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"....a distinct advance in the treatment of scabies".*

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* Wooldridge, W. E.: The Gamma Isomer of Hexachlorocyclohexane in the Treatment of Scabies, J. Invest. Dermat. *10*:363 (May) 1948.

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Heart Failure of Pulmonary Origin

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BEFORE considering right heart failure consequent upon disturbances in the lung circulation, it is well to be reminded that the commonest cause of right heart failure is left heart failure. Bloomfield, Cournand and their co-workers (1946) have, in fact, demonstrated that the pressure in the pulmonary artery in mitral stenosis may rise to over 100 mm. mercury, a level well above that which occurs in cases of emphysema. In differential diagnosis some of the common congenital faults such as interatrial septal defect and pulmonary or subpulmonary stenosis have to be kept in mind. We have seen very complex conditions arise when such congenital defects have become complicated by acquired severe lung disease.

A useful working classification of the causes of pulmonary heart disease is given in the table. In pathogenesis there are two main factors:

1. *The obstructive factor.* This is most clearly exemplified by massive pulmonary emboli, which pack the branches of the pulmonary artery, producing a gross reduction in blood flow, and an acute, often disastrous, state of collapse. Less massive, but oft-repeated embolization from tumors or recurrent thrombosis of leg veins may produce a clinical picture which is less dramatic; slowly progressive breathlessness with evidence of right heart enlargement are then the main signs. In certain places in the tropics where schistosoma infections are important, the ova may get into the systemic circulation and block the lung vessels. Although right heart hypertrophy and pulmonary artery enlargement are common, death from consequent heart failure is surprisingly unusual.

2. *Pulmonary anoxia.* Motley and others (1947) and also von Euler and Liljestrand (1946) have shown that a reduced oxygen tension in the lungs will raise the pulmonary artery pressure very considerably. It seems likely that this mechanism may contribute in such conditions as kyphoscoliosis. It is well recognized that pulmonary ventilation becomes seriously impaired in patients with gross deformity of the thorax, and patients frequently die with signs of right heart enlargement and failure. Examination of the lungs in such patients reveals no anatomical causes of vascular obstruction, and there are many instances in which there is no bronchitic element. It is clear that some functional disturbance must be postulated and the arteriolar constrictive reaction to low oxygen tension may be a clue. In the anoxic group of pulmonary heart disease, the arterial blood oxygen saturation is found to be reduced from the normal 95 per cent to below 80 per cent. This reduction of available arterial oxygen brings in a further cardiovascular reaction similar to that in anemia: the cardiac output is often increased above the resting level, and this constitutes a further load on the heart.

Very frequently the factors of vascular obstruction and anoxia are mixed. In silicosis one may see a type

TABLE 1.—*Classification of the Causes of Pulmonary Heart Disease*

1. ACUTE: Massive pulmonary embolism.
2. SUBACUTE: (a) Lymphatic miliary carcinomatosis.
   (b) Embolic carcinomatosis.
3. CHRONIC: A. *Lung Disease.*
   (a) Emphysema heart disease, due to
      (i) Bronchitis
      (ii) Bronchiectasis
      (iii) Cystic disease
   (b) Fibroid lung, due to
      (i) Tuberculosis
      (ii) Sarcoidosis
      (iii) Scleroderma
   (c) Pneumoconiosis, due to
      (i) Silicosis
      (ii) Anthracosilicosis.
   B. *Vascular Disorders of the Lungs.*
   (a) Primary pulmonary hypertension
   (b) Recurrent pulmonary embolism
   (c) Schistosomiasis.
   C. *Kyphoscoliosis.*

Presented October 28 before the Nineteenth Annual Postgraduate Symposium on Heart Disease of the Heart Division of the San Francisco Tuberculosis Association, and November 5 before the Eighteenth Annual Postgraduate Symposium on Heart Disease of the Los Angeles Heart Association.

of endarteritis in the vessels which is present along with gross lesions which probably impair pulmonary ventilation. The work of Hickam and Cargill (1947) has shown an apparent rigidity of the pulmonary vascular bed in emphysema.

CLINICAL MANIFESTATIONS

1. *Acute cor pulmonale.* Packed pulmonary emboli commonly complicate severe medical or surgical illness. With or without warning symptoms of small peripheral pulmonary emboli, the patient suddenly develops circulatory collapse with a feeling of air hunger and substernal oppression. The venous pressure is raised in the neck veins, while the circulation is severely reduced with accompanying pallor, sweating, pulse of small volume and reduced blood pressure. The veins in the neck are engorged, but careful inspection in the early stages may be necessary to perceive this sign. Exaggerated pulsation over the right ventricle and possibly a gallop rhythm may be noted. The electrocardiogram will reveal evidence of acute right ventricular strain and even the acute development of a right bundle-branch-block pattern.

Practically the only other acute vascular collapse which may simulate this condition results from rupture of the aorta into the pericardium. Here, also, we encounter peripheral collapse with a raised venous pressure.

2. *Emphysema heart.* This condition, in our experience, is by far the commonest variety of pulmonary heart failure. Most of the patients are over 40 years of age, and there is a considerable preponderance of males, in my experience nine to two. The breathless bronchitic, whose dyspnea persists between attacks, has advanced to a stage at which emphysema is sufficiently pronounced to interfere with the normal oxygenation of his blood. Attacks of giddiness and fainting commonly occur at this stage.

Sooner or later evidence of right heart hypertrophy, and then failure with congestion and edema, will complete the picture. The patient is dusky blue, and his veins are congested; but in contrast to the patient with low output heart failure, whose extremities tend to be cold and blue, the hands, nose and ears are usually warm. The pulse is rapid (90-120) and is of good volume, as might be expected from the slightly raised cardiac output. A curious and interesting feature is the occasional presence of papilledema and retinal hemorrhages. Complicating exacerbations of bronchitis are often present and seem to be precipitating factors in determining failure. When there is accompanying asthma or bronchiolitis the patient is orthopneic, but in some striking cases, without associated bronchial obstruction, he may be most comfortable in a completely recumbent position, even though venous engorgement is gross. Terminally hydrothorax and edema may develop at the lung bases, a mechanical explanation of which is not easy to conceive. The cardiac output is usually falling at this stage and a general cardiac failure of a maloxygenated heart may be part of the terminal picture.

Apart from evidence of right hypertrophy, which may be difficult to detect clinically as the heart is often concealed by enlarged lungs, there is little to be made out on physical examination of the heart. Triple rhythm may sometimes be audible to the left of the sternum. A diastolic murmur of pulmonary insufficiency is rare. Radiologically, enlargement of the pulmonary artery is common, but it is only occasionally that right ventricular hypertrophy can be recognized with certainty in the roentgenogram. The electrocardiogram shows evidence of right ventricular preponderance, and this is often present before the other signs of right heart failure develop. Auricular fibrillation, an almost constant accompaniment of failure in mitral stenosis, is exceptional in emphysema heart, occurring in only about one case in ten.

The arm-tongue circulation time is normal. Polycythemia is unusual, but it does occur sometimes. It is perhaps worth noting that the arterial oxygen reduction may be much greater in severe congenital heart disease than in emphysema, and the bronchial infection in the latter condition may possibly interfere with bone marrow activity. Blood alkali reserve is often raised and plasma chloride correspondingly reduced.

3. *Acute circulatory failure from sudden reduction of negative intrathoracic pressure.* Patients with emphysema who develop a superadded pneumothorax of the valvular variety, or who have a large bulla which may blow up in a similar manner, are likely to become acutely distressed with severe dyspnea, gross air-hunger, and a pulse of poor volume and low pressure. In one such emphysematous patient who had pneumothorax the intrathoracic pressure fluctuated around zero, while the hydrostatic pressure in the right auricle remained extremely low. Filling of the heart, which normally takes place at an effective filling pressure of 7 cm. water (2 cm. hydrostatic pressure plus 5 cm. negative intrathoracic pressure) was grossly interfered with, and the cardiac output was 2.4 liters per minute (normal 5.3). In spite of the low output in this particular patient there was electrocardiographic and clinical evidence of right heart hypertrophy, showing that the raised pulmonary resistance is independent of the high cardiac output factor. This is a variety of acute circulatory failure which of course is easy to differentiate from chronic cor pulmonale with venous congestion.

4. *Other clinical varieties.* Patients with right heart failure must be subjected to detailed study if the causal factors are to be completely comprehended. Sometimes these may be obvious on radiological examination of the chest. Silicosis, tuberculosis, or non-tuberculous fibroid lung may be recognized. Among the rarer causes are the following:

Sclerodactyly. In this condition, the skin over the fingers becomes thickened and this is associated, in the early stages, with undue coldness and blanching on exposure to cold (Raynaud phenomenon). Along with this, there are other features such as rarefaction of the terminal phalanges, subcutaneous calcinosis, pigmentation of the skin, and visceral affections of the esophagus, lungs and heart. A diffuse fibrous change affects the walls of the alveoli; right ventricular preponderance and breathlessness may develop.

Recurrent pulmonary embolism was first recognized by Ljungdahl (1928) and my own experience would confirm this as a clear entity. Progressive dyspnea and pain over the liver are the major symptoms. It is noteworthy that the patients may have little pleural pain and no hemoptysis. Electrocardiograms show evidence of right ventricular hypertrophy together with distention of the pulmonary arteries. Pathologic changes consist of gross hypertrophy of the right ventricle with recent as well as old organized and recanalized emboli in the lung arteries.

Secondary carcinoma in the lungs. A widespread dissemination of secondary cancer may take place through the bloodstreams or along the peribronchial lymphatics. These modes of spread may affect the lungs in different ways; tumor cells within the lung vessels may be associated with surrounding thrombosis and organization. Lymphangitis carcinomatosa may be associated with obliterative endarteritis as a result of invasion of the vessel walls by growth. In these instances the right heart stress results from obstruction of the lung vessels. A suffocating form, however, occurs as distinct from the vascular obstructive variety, and this may, of course, lead to the anoxic type of pulmonary heart failure. In these cases the cancer is usually of a scirrhous type with contraction of scar tissue around the bronchioles and perhaps even invasion of the bronchial lumen by growth. In such instances the raised venous pressure is accompanied by rapid circulation, warm hands and a full bounding pulse.

Primary pulmonary hypertension. There are now in the literature many instances of failure of the right ventricle with associated pulmonary vascular sclerosis, usually described as cases of primary pulmonary hypertension. The sclerosis in these cases affects the small arteries of the lungs, which are usually spared in mitral stenosis. The diagnosis rests on the exclusion of other causes of pulmonary artery enlargement. By means of right heart catheterization the pressure in the right ventricle is found to be greatly raised, and the pulmonary arterial pressure itself, when measured, is raised to figures like 80-100 mm. mercury. Postmortem studies on such patients are often somewhat obscured by the coincidence of numerous pulmonary emboli, which complicate this and all other varieties of terminal heart failure with such great frequency.

Treatment. As in most other diseases the key to good treatment is the recognition of the cause, and an understanding of the underlying mechanisms. In the obstructive variety due to packed pulmonary embolism the essential therapeutic measure is the prevention of further leg vein thrombosis and consequent embolization of the lungs. Anticoagulant remedies such as heparin by injection, and dicumarol by mouth, with proper attention to control of coagulation times, are indicated. The high venous pressure is probably part of the mechanism maintaining blood flow from the right heart through the lungs, and its reduction by venesection or digoxin is undesirable. Patients should be kept quiet with morphine, and if no further embolization takes place, excellent and complete recovery, with restoration of electrocardiographic changes to normal, can take place in a few weeks.

In the anoxic form, best exemplified by emphysema, it is important to keep in mind that the high venous pressure is probably also a compensatory phenomenon maintaining the necessarily raised cardiac output. Venesection and digoxin may do harm; the inefficacy of digitalis preparations in pulmonary heart disease was recognized by Vaquez (1928) as a result of many years of astute observation of clinical results. He recognized that strophanthin preparations, particularly ouabain, might have some beneficial action in these patients, and we now have a good deal of experimental evidence in support of that observation.

The most successful measure in treatment, however, is use of an oxygen tent. By raising the arterial oxygen saturation, the excessive strains on the right ventricle seem to be lifted. If the patients are kept in a tent, for weeks if need be, one may see the most dramatic recoveries in conditions which at first appear almost hopeless. If the patient can be kept alive until the causal exacerbations of bronchitis have subsided the asphyxial condition becomes more and more easy to relieve. If there are any potent remedies for the superadded bronchial infection, they should be used. Our own experience, however, has been disappointing in this respect. Penicillin inhalations simply alter the bacterial content of the sputum without notably shortening the illness.

The right heart tolerates an overload less easily than the left. This has been shown experimentally by Müller (1937) and it may have something to do with the fact that an increased aortic pressure load on the left ventricle automatically increases the blood supply to the heart through the coronary arteries which take origin from the base of the aorta. No such automatic increase takes place when the right heart is subjected to pulmonary hypertension. Patients with pulmonary heart disease, therefore, are always in a precarious condition and, if the disease is one of the chronic forms, they do not readily tolerate more than one or two attacks of failure.

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CAUSALGIA

A Review

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"Causalgia defies every therapeutic method with an obstinacy that drives one to despair."—TINEL.

PERCIVAL POTT mentioned "certain painful afflictions of the nerves" in connection with injuries of the extremities, but it was not until 1813 when Alexander Denmark[9] reported a case that causalgia was clearly described. The patient, a soldier, had been struck by a musket ball just above the inner condyle of the humerus with a resulting radial nerve palsy. Denmark described the intense burning pain, the prostration, the trophic changes, the loss of function and even a tender nodule at the site of the wound. He believed that relief might follow section of the nerve above the level of the lesion, but at the insistence of the patient and with the advice of his colleagues the arm was amputated. Complete relief was reported. Denmark's dissection revealed a lacerated but not divided nerve, intrinsic and extrinsic scar, as well as a tiny fragment of lead embedded in the nerve.

In 1864 James Paget[34] gave a brief, clear and forceful account of the disorder which was cited by Wier Mitchell[31] in his more generally recognized and more complete report later in the same year. Mitchell's description is widely hailed as a classic and even today is extensively quoted, often with an appended comment that nothing has been added to the description since. While the general truth of such homage is not to be denied, the force and lucidity of Mitchell's description at times outstrip the absolute accuracy of his observation. One may attempt, therefore, to replace the traditional introduction to the nosography of causalgia with a summary of those factors which have been found to appear repeatedly in the reports of later observers.

Attention should be drawn to the widespread lack of agreement over clinical definition. The terms causalgia, major causalgia, reflex sympathetic dystrophy, thermalgia, synesthesialgia, post-traumatic painful state, painful osteoporosis, Sudeck's atrophy, and the causalgic state are all used with varying degrees of discrimination. Moreover, the so-called minor causalgias may or may not be included in one of these terms. Finally, the minor causalgias are variously defined. Some consider them to be characterized merely by relatively slight involvement and suffering; others reserve the term for more or less well defined clinical entities such as Sudeck's atrophy or post-traumatic osteoporosis. De Takats[44] calls for a redefinition, stating that frank causalgia is readily recognized but that there are a variety of related afflictions dependent upon the same neural mechanisms which are readily and commonly misunderstood. Evans[11,12] considers that causalgia is a misnomer, as does Stoppford,[43] and states that burning pain may or may not be present. Homans[18] suggests that true causalgia is seen only in injuries to major nerves and that other similar disorders which are usually due to relatively minor injuries be grouped together under the term "minor causalgia." Insofar as possible this classification will be followed in this presentation.

On the major clinical features all authors are in agreement. These include burning pain, trophic changes, failure of the pain to remain within the bounds of the distribution of the affected nerve, profound physical and psychical deterioration, the tendency to paroxysms of pain and to aggravation of pain by emotional stimuli. Today many would also include instant, if but temporary, relief following sympathetic block in the list of essential diagnostic criteria. The Medical Research Council in 1920 set up the following as the essential characteristics of causalgic pain: (1) spontaneous; (2) hot and burning, intense, diffuse, persistent, but subject to exacerbations; (3) excited by stimulation which does not necessarily produce a physical effect on the limb; (4) aggravated by emotional excitement which usually brings on a paroxysm. Mayfield[29] (1947) states that the diagnosis can always be made when there is (1) burning pain associated with trophic and vasomotor changes in an extremity following a peripheral nerve injury; (2) aggravation of the pain by emotional stimuli; and (3) instant relief following sympathetic block.

On other points there is less agreement. Mitchell[32] reported the disorder as being present in 19 of 50 peripheral nerve injuries which came under his observation. At the other extreme, Carter[8] in an excellent and thoughtful paper (1922) reported true major causalgia present in only four of 3,000 peripheral nerve injuries. In an attempt to establish a reasonable figure for the overall incidence, figures have been combined from eight reports that give evidence of accuracy and freedom from obvious sampling errors. Neither Mitchell's nor Carter's figures are used. From these papers there were culled 140 cases of *major* causalgia occurring among 3,326 cases of peripheral nerve injury, an incidence of 2.1 per cent.

There is a similar lack of agreement as to the distribution of causalgia through the various major nerves. The earlier authors, with varying degrees of rigidity, uniformly label causalgia primarily a disease of the median and sciatic nerves. Reports from the most recent war do not entirely support this. Thus, Rasmussen and Freedman[37] in a series of 100 cases report involvement of the median nerve

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in 17, multiple nerves in 17, brachial artery and great nerve in 11, brachial plexus in 10, ulnar nerve in 9, radial in 6, and sciatic in 8 cases. Freeman[14] reports that in 91 cases the radial nerve was affected in 18, the median in 15, the ulnar in 13, the brachial plexus in 11, and the sciatic nerve in 5. From about 200 cases reported by five authors composite figures reveal involvement of the median nerve in 25 per cent, the sciatic in 22 per cent, the brachial plexus in 18 per cent, the ulnar nerve in 14 per cent, the radial in 12 per cent, the posterior tibial in 5 per cent, and the peroneal nerve in 3 per cent. These percentages are indicative of the incidence of causalgia in a given nerve in relation to other major nerves, and not of the frequency in relation to all causalgic states. This is the only figure that one can supply that is not subject to the sampling errors of local combat factors, differences in diagnostic criteria and other variations.

Mitchell reported that pain always appeared some time after the nerve injury and innumerable accounts since then have contained the same statement. Leriche[22] denied this and cited a case of causalgia in which the injury occurred in his presence and in which the characteristic burning pain appeared immediately. Rasmussen and Freedman state that 48 of 100 patients had burning pain within six hours, and Ulmer and Mayfield[49] report the typical burning pain as being present from the instant of injury in 44 of 100 cases.

Whether or not causalgia may occur in the presence of a completely severed nerve is likewise unsettled. The preponderance of opinion is that it does not, and many who express such a view are extensively acquainted with the subject. Carter, Leriche, and Ulmer and Mayfield have all found for the negative. However, Allbritten and Maltby[1] report two cases of causalgia, and Bondarchuck[6] reports one more, occurring in the distribution of a completely divided nerve.

The underlying pathological and neural mechanisms have long been a source of controversy and conjecture as well as research. While the remarkable penetrations of Wier Mitchell into the subject are well known, attention may be directed to Létiévant[23] who, though less well known, is no less profound. In an extraordinary monograph which appeared in 1873, Létiévant discussed causalgia and related painful states with rare insight.

He stated that in such conditions there are three anatomical sites fundamental to the mechanism: the peripheral nerve and its point of irritation, the spinal centers, and the sensorium. He stated that theoretically the pathological activity could be interrupted at any of the three sites, but that the only one surgically accessible (in his day) was the peripheral nerve. The steps he listed in the development of the abnormal mechanisms are:

1. Local irritation due to the injury.

2. Transmission of impulses from this site to the spinal centers.

3. Here, in the spinal centers, if the impulses are strong enough and sustained long enough a state of abnormal neural activity appears and spreads to adjacent centers.

4. Having produced this spread, not only do the usual impulses ascend to the sensorium, but other impulses which have arisen in the adjacent disturbed areas ascend, producing an extraordinary amount of painful sensation.

5. The spread to adjacent areas likewise causes the associated peripheral phenomena.

Létiévant states that neurotomy interrupts the irritating impulses and that while the abnormal neural activity may reverberate throughout the neuroaxis for a time, usually this dies out and relief then follows.

In 1916 Leriche[20] proposed that the underlying abnormality is a perversion of sympathetic activity and that treatment therefore should be directed to the modification of the sympathetic system. Later in the same year Meige and Athanassio-Bénisty[30] presented clinical, physiological and histological evidence in support of such a concept. By 1921 at least, Tinel[46,47] had subscribed to the same view.

In 1917 Stoppford[43] reported two constant pathological findings, partial division of the nerve and interstitial fibrosis, findings which have since been shown to be nonspecific.

Carter[8] reviewed the subject and discussed the possible reasons why the median and sciatic nerves were so susceptible to causalgia. These were given as: (1) both supply special peripheral areas rich in sensory endings, (2) both contain large vasomotor components, (3) both have large intrinsic arterial supplies, and (4) both supply a large arterial arch with large numbers of vasomotor fibers. He also discussed the theories then prevalent and in greater or less degree deflated all. These were (1) paralysis of vasoconstrictors, (2) irritation of vasodilators, (3) abnormal reflex activity, (4) sympathetic abnormalities, and (5) alteration of vascular supply to the median or sciatic nerves.

While causalgia and allied states are seen in industrial and private practice, it is most frequently seen in soldiers. Interest waned between wars, and Carter's paper which appeared in 1922 was the last of importance until just before the last war.

However, during this interval an enormous development in neurophysiology prepared the background against which new cases, which were to appear in such numbers, might be viewed. Understanding has progressed along two main lines; broadly, central mechanisms and peripheral mechanisms. Of these, the former is most widely discussed, most heavily called upon and perhaps most articulately and reasonably expressed by Livingston.[24] The other, the peripheral mechanism, with the striking exceptions of a few papers, remains merely a "seat of irritation," an initiating focus which is all too quickly dismissed in the hasty ascent to higher centers. If, in the discussion to follow, we may temporarily defer Livingston and

Doupe, Cullen and Chance, we may more sympathetically attend other views.

Moser[33] in 1943 proposed that the intimate mechanism lies in the continuous excitation of afferent sympathetic paths which set up an irritation in the thalamus such that peripheral stimuli of all kinds are translated into pain which is referred to the affected limb.

De Takats[44] in 1945, calling on Kinnier Wilson, stated that sensory pathways should be regarded as being susceptible to stimulation at all levels. He proposed that the initial lesion affects the first neuron, which may itself initiate vasomotor reflexes that are predominately vasodilator, as shown by Bayliss.[3] If not treated promptly or properly the disturbance will then ascend to the second neuron which he appears to consider as being in the spinal cord. The third neuron he regards as being in the cerebral cortex, and he stated that under the constant barrage from lower centers the cortex might then become the "seat of projected, self-propelled impulses to the periphery."

Zikeyev,[52] in 1946, stated that miraculous cures are not to be expected because the thalamus is implicated in the ultimate neuropathologic process. He feels that there are two factors in the neural structure of causalgia, a persistent irritation at the site of the injury and a dysfunction of the thalamus. He suggested that the essential striking feature of causalgic pain is its thalamic nature as evidenced by its tendency to spread, even to the whole half of the body, the paroxysms, the psychic effect. He employs Pavlov's concept of preserved inhibition, stating that in causalgia the thalamus and related cortical cells lose this preserved inhibition which is normally maintained by rest and the attendant lack of afferent bombardment.

Rusinov,[38] in 1947, reported peculiarities of action currents from the median nerve of a patient with causalgia. Painful irritation produced an electrogram which differed from electrograms of normal subjects in that there were bursts of relatively high voltage spikes occurring in groups. He feels that this alteration is due to intensification of impulses as they pass the point of damage. One is led to the inference that this intensification is the neuropathological basis of the disorder.

To return to Livingston[24] and the physiological background upon which he draws, we may briefly recall the salient points of Lorente de No's[26] 1938 discussion of the internuncial pool concept. Lorente de No stated that the nervous system contains enormous numbers of interlacing paths with numerous opportunities for the conduction of impulses over divergent routes. During activity these paths are functionally segregated into active and inactive groups. The active groups arrange themselves in convergent chains of relatively simple patterns of which there are but two types, the multiple and the closed. He stated that the mechanism of stimulation of neurons is the delivery of impulses at their synapses. The effect of individual impulses is brief, but the continuous arrival of impulses insures constant stimulation. The neuron responds whenever the simultaneous effect of the impulses that arrive within a period of effective summation reaches its threshold.

Fractionation of internuncial paths and failure of "avalanche discharge" depend upon the rigidity of conditions necessary for any neuronal discharge. In order to have effective summation and discharge, a neuron must have a sufficient number of spacially remote synapses which are activated all at once. Cells in the active chain fulfill this requirement; those in the inactive chain remain on the subliminal fringe.

Lorente de No then illustrated how a neuron which originally could have been fired only by the simultaneous appearance of impulses at two of its synapses may continue to fire even when one of the original exciting impulses drops out. This is due to a closed chain circuit which, as part of its activity, partially excites the neuron in question.

With this in mind we may now summarize Livingston's discussion. He proposed that in causalgia a partial lesion of a nerve is followed by a focus of irritation which transmits to the cord a sustained barrage of impulses that serve to upset the normal functioning of the internuncial pool. The path of incoming impulses is so altered by this abnormal activity of the pool that the pattern of excitation, eventually registering in consciousness, is changed. Continued pool activity in time implicates the anterior and lateral horn cells; the changes in muscle and vasomotor activity resulting from this furnish new sources for pain impulses. Finally, as the intensity of this self-sustaining process is increased, other more distant neurons throughout the central nervous system are drawn into the complex. In speaking of the vicious circle concept he recognizes three components: incoming impulses from the periphery, internuncial pool activity, and motor impulses from the lateral and anterior horns. Of these, if any may be said to be more important, it is the internuncial pool.

Porter and Taylor[35] (1945) reported what they termed a "facilitation reflex" and offered it as partial support of Livingston's discussion. Under experimental conditions they showed that reflex motor response to constant minimal induction shocks to a sensory root of a cat is greatly facilitated by other sensory impulses such as heat or cold or even blowing on the fur.

To turn to the concept of a peripheral mechanism, one finds a report by Katz and Schmitt[19] in 1942 showing that under certain experimental conditions action currents in nerve fiber can initiate impulses in an adjacent fiber. In 1944 Granit[16] and co-workers showed that in isolated sections of peripheral nerve in cats impulses traveling in a motor fiber were capable of initiating impulses in adjacent sensory fibers. Employing the term "artificial synapse" they show that the same phenomena are encountered when such a nerve is partially dam-

aged or crushed. They suggested that these facts might well be fundamental to the pathological activity in causalgia.

With this and similar corroboratory evidence in mind, Doupe, Cullen and Chance[10] in 1944 postulated that causalgic pain might well be due to activation of somatic sensory fibers by efferent sympathetic impulses. They pointed out that sympathetic impulses to digital vessels and palmar sweat glands are greatly increased by emotional stress; moreover there is more or less constant activity in sympathetic fibers in response to thermo-regulating needs, postural activity and pilomotor activity. As a result the pain would appear to be spontaneous, yet would be sharply increased with emotional changes or with pain elsewhere or with respiration, all of which are known to increase both the pain in causalgia and efferent sympathetic impulses. Such a mechanism likewise explains the diffuse character of the pain. Also, pain and temperature fibers, being small, might well be particularly susceptible to sympathetic fiber action currents. If this were true it might explain the burning pain. Finally, it affords a clear-cut explanation of the relief of causalgic pain following sympathetic block.

They pointed out that all observations may be explained on this basis, vasomotor and trophic changes being explicable through antidromic stimulation of afferent fibers. The variable time of onset and the tendency for symptoms to fade, they felt, must be explained by the peculiar and intimate structure of the peripheral leak between the sympathetic and sensory fibers.

This seems a striking and stimulating paper, but so are the views of those who champion the internuncial pool as the fundamental mechanism in causalgia. But each concept, it seems, is incomplete. There are clinical observations which each viewpoint neglects to scan. All will agree that there is some unusual dominating neuropathologic mechanism at work which, by virtue of its own unique capacities, forces the causalgic state into existence. The internuncial pool concept is a useful clinical projection of basically sound neurophysiology. Yet why should one man's internuncial pool become pathologically active and another's not? Or is it to be supposed that this pathological activity springs up full blown in those cases which are marked by burning pain from the outset?

Similarly the concept of an essentially peripheral mechanism as presented by Doupe, Cullen and Chance fails to account for those cases which do not respond to sympathectomy. Nor does this theory explain mirror image phenomena nor other types of unusual spread.

It seems that each concept contains that which the other lacks; that each bears powerful support of its own implication. The one great flaw in the internuncial pool concept is its failure to explain adequately the onset—the first, the basic neuropathologic error. Thus, the artificial synapse could provide the unique, though rarely observed, basic abnormality; the internuncial pool could modify this and in certain cases maintain a self-exciting pathological pattern.

We would conceive of the process something like this: One hundred men, normal, healthy, receive wounds damaging their median nerves; ninety-eight display palsy of various degrees but nothing more. But in the remaining two the intimate and so far inscrutable micro-anatomical derangement will be such that abnormal function appears. The insulation, so to speak, has been carried away but the thus bared conducting mechanism retains its power of function; efferent sympathetic impulses induce action currents in adjacent somatic afferent fibers; pain of a distinctive and baffling nature appears; the patient finds that any activity associated with sympathetic discharge increases the pain. The vicious circle is already in force and the clinical picture continues to develop. One of the two may have the sympathetic outflow blocked early and obtain relief. The other may not, and the continuing whirlpool from lateral horn to the periphery to the posterior horns to higher centers to lower centers and back to the lateral horns draws ever more neurons into the vortex. Finally, interruption of peripheral sympathetic efferents is not followed by relief; the closed chain circuits have taken over and the process is self-exciting.

METHODS OF TREATMENT

Treatment has so progressed since Tinel's time that his company is now rarely sought by the misery of despairing surgeons; yet many, in sorrow still recall that:

> *"Diseases desperate grown*
> *By desperate appliance are cured*
> *Or not at all."*

The first treatment was Denmark's amputation. Mitchell employed blisters; Létiévant, neurotomy. Sicard[40] used intraneural injections of 60-per cent alcohol, as did Turco,[48] Dean Lewis[25] and others. Stoppford advocated section and end-to-end suture; Stoffel[42] used what we would call neurolysis. Some successes are reported for all of these methods. Modern methods may be considered to have begun with Leriche who developed periarterial sympathectomy and segmental arteriectomy. Today, as is well known, treatment is almost uniformly sympathectomy by one means or another.[2,5,7,15,17,21,39]

In 1943 White[50,51] reviewed the treatment of causalgia and concluded that neurectomy, posterior rhizotomy and intraneural alcohol were of no value; that excision of a neuroma was worth one trial but no more; that sympathectomy was excellent, and that cordotomy was often very much worth while.

In 1945 Speigel and Milowsky[41] reported nine cases. All the patients received complete but temporary relief from procaine blocks. One was so improved by one block that nothing further was done. One obtained complete relief from alcohol block, and the other seven were completely relieved by preganglionic sympathectomy. Machabeli,[27] in

1945, reported complete relief in 23 of 25 patients by what he terms "fasciculation," which appears to be a neurolysis.

De Takats[44] in 1945 reported on 54 patients treated in keeping with his concepts. Thirty-six were treated with local procaine with relief; he considered these cases examples of first neuron involvement. Twelve were treated with sympathectomy on the assumption that these were examples of the second stage first neuron class; these 12 obtained relief. There were six patients that he considered to be examples of the second or third neuron class who did not respond to sympathectomy or, in two cases, to cordotomy. Of these, one killed himself, two are in asylums and three are morphine addicts.

Mayfield and Devine[28] reported 15 cases in 1945. Five of the patients had neurolyses, three periarterial sympathectomy. None benefited. Twelve had preganglionic sympathectomy; all obtained complete relief.

Mentioned only to be condemned is a 1945 report of cure of a patient with causalgia by psychotherapy. The appended case history will not support the diagnosis of causalgia.

In 1946 Rasmussen and Freedman[37] reported 100 cases. Of 91 who received procaine blocks, 73 obtained complete temporary relief, 16 marked temporary relief and two showed no change. Of the 91, thirteen obtained complete permanent relief from blocks alone, while 32 more obtained moderate permanent relief. Postganglionic procedures were employed in 21 patients with involvement of the upper extremity and 14 of these obtained total relief; but 13 of 14 patients received total relief in the upper extremity after preganglionic procedures. Moreover, four-fifths of the patients with causalgia of the lower extremity retained some pain after lumbar ganglionectomy.

Ulmer and Mayfield[49] in 1946 reported 75 patients. In two cases the nerve was resected and sutured, with cure. Seventy had sympathectomy. Of these, seven were not completely relieved until a second procedure taking more ganglia was carried out; the remaining 63 patients were completely relieved after the first procedure.

Berry[4] and associates studied tetra-ethyl-ammonium bromide in various disorders including causalgia. Without giving much clinical detail, they stated that it is as effective as sympathectomy—temporarily.

Evans[13] reported 57 patients observed in the Lahey Clinic. Twelve had sympathetic blocks only, 11 with satisfactory to complete relief. Twenty-nine had sympathectomy. Eleven had complete relief, 11 more had 50 to 90 per cent relief, but seven were unchanged.

Rasmussen and Alessi[36] reported the use of Rectocaine, a slowly absorbed local anesthetic, in two cases of causalgia. The first patient displayed complete sympathetic paralysis in the expected area for two weeks and complete freedom from pain for the period of the follow-up which was only ten weeks. The other's sympathetic paralysis lasted for three weeks and there was freedom from symptoms for the period of the follow-up.

In 1946 Allbritten and Maltby[1] reported 67 cases. Sympathectomy was carried out in 30 patients, 28 of whom obtained relief reported as good to excellent. The other two experienced no change.

Zikeyev[52] supplied an interesting report of 37 patients in 1946. It is Zikeyev who believes that the thalamus is so thoroughly involved in the neuropathology. Treatment was surgical followed by prolonged narcotic sleep which was continuous with and immediately followed the anesthesia. It was maintained for five to six days by a nostrum, modestly called "sleeping mixture," which contained sodium bromide, chloral hydrate, tinct. valerian, luminal and pantopon. Of the 32 patients so treated, 31 were completely relieved and one moderately so. However, these figures become somewhat less imposing when the operative procedures are reviewed. Eleven had resection and suture of the nerve, 13 had resection and graft, and eight had neurolysis. And it is known that nerve section is followed by relief in a high percentage of cases.

Mayfield[29] reported 105 cases in June, 1947. He now uses procaine block for diagnosis only. He employs the Smithwick preganglionic procedure for the upper extremity and removes the second and third lumbar ganglia for the lower extremity. Of the 105, all but nine were relieved completely by the first procedure. All of the nine were relieved by a second slightly more extensive procedure.

Freeman[14] in July, 1947, reported 114 cases. All responded temporarily to procaine blocks, but only the mildest cases responded to repeated procaine blocks with permanent and complete relief. The first two patients were treated with preganglionic resection, below the third thoracic and rami of the second and third. These were completely relieved, but only for one week. The stellate and the second and third thoracic ganglia were removed in the next four cases. Two patients showed excellent results, in another the result was fair, but in the fourth poor. The next seven had the stellate, second and third thoracic ganglia and the intervening chain removed and the periarterial sympathetics removed from the subclavian artery. All obtained complete relief of pain; two had excellent functional recovery, but in the other five the peripheral soft tissue changes were so great as to preclude good functional recovery. The next ten patients were treated in this manner but very early. All obtained complete relief and eight returned to duty. The next four patients were treated with early peripheral surgical operation followed by repeated procaine blocks, all with excellent results.

SUMMARY

The literature of causalgia is briefly reviewed.

The various theories of possible underlying mechanisms are examined.

The view is advanced that both the theory of peripheral mechanisms proposed by Doupe, Cullen and

Chance and the internuncial pool concept are fundamental to the complete elucidation of the intimate neuropathology of causalgia.

The results of treatment as reported by various authors are summarized.

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The Surgical Significance of Acute Abdominal Pain

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IN reviewing my observations in two of the larger hospitals of New York over a period of 25 years, I have been disturbed by the frequency with which patients suffering from acute abdominal pain are subjected to laparotomy with resulting negative pathologic findings. Even more distressing is the opinion expressed by many surgeons that exploration with negative findings is preferable to unrecognized acute appendicitis which may develop into peritonitis with a fatal termination. We cannot but question this attitude in view of the present minimal mortality rate from acute appendicitis, including cases with abscesses and general peritonitis.

In a review of acute appendicitis on the fourth division of Bellevue Hospital over a 12-year period from 1928 to 1939, inclusive, we[8] found the mortality rate during the first six years, namely, 1928 to 1933, to be 6.3 per cent and from 1934 to 1939, inclusive, 3.4 per cent. The total mortality rate of 677 patients suffering from acute appendicitis was 5.1 per cent. The diagnosis was based entirely on the findings of the pathologist and not on the findings of the operating surgeon. Among these 677 patients there were 474 cases of unruptured acute appendicitis, 67 cases of localized peritonitis, 88 abscesses and 48 cases of general peritonitis. In 75 per cent of the cases the operations were performed by the house staff, and the junior attending staff performed the other 25 per cent. These statistics represent the results before chemotherapy was instituted.

From 1940 to 1947, inclusive, there have been 265 operations for acute appendicitis with the same percentage of peritonitis and abscesses, the resident staff performing nearly all the operations. There have been four deaths, three of which were caused by cardiac insufficiency. This is a mortality of 1.5 per cent, which eliminates the great fear of death from acute appendicitis. Reasons for the diminished mortality rate include the use of chemotherapy, the more frequent use of plasma and blood and keeping the patient well hydrated at all times. Improved anesthesia and a more careful follow-up by a better trained resident staff are important advances.

Dr. Edgar Burke, surgical director of the Jersey City Medical Center, has been kind enough to allow me to quote his statistics on acute appendicitis for 1947 which include those cases with general peritonitis, local peritonitis, and abscess. The total number of patients operated upon during the year 1947 was 271, with one death or a mortality of 0.36 per cent. These figures are most impressive when one considers that the resident staff performed nearly all the operations.

In attempting to analyze the reasons for frequency of the mistaken diagnosis of acute appendicitis in acute abdominal pain, we naturally attribute most of these errors to the lack of clinical experience of younger surgeons. From my observations I have found this to be true. However, I feel that an additional factor is the basic training of the young surgeon while serving his residency. If he is taught that exploratory laparotomy is indicated in most cases of acute abdominal pain, then such will be his practice.

During the past eight years I have served on the committee on applicants of the American College of Surgeons for New York City. In this capacity I have had opportunity to note that many young surgeons when interviewed present a list of operations done during the preceding year which includes a percentage of appendectomies out of all proportion to the total number of operations. For instance, a surgeon applying for a fellowship in general surgery may present a list of 60 to 100 operations, of which 25 to 35 per cent are for acute or chronic appendicitis. The members of the committee feel that the candidate's percentage of appendectomies is probably four to five times greater than that of the members of the committee.

The teaching of three to four decades ago was to impress upon the clinician that acute abdominal pain represented an acute pathologic process which usually necessitates a laparotomy. We were told that the appendix was the most frequently diseased organ we had to fear. This teaching has become so thoroughly implanted in the mind of the surgeon, and to a great extent in the mind of the internist, that a patient suffering from acute abdominal pain is usually regarded as a candidate for laparotomy. Frequently the operation reveals negative findings.

Certainly a patient with acute abdominal pain should not be rushed into a laparotomy unless there are clear-cut indications that a real pathologic process is present.

Acute abdominal pain may be attributed to three causes.

1. Anxiety neurosis with conversion symptoms or other psychogenic factors.
2. Physiologic conditions, such as painful ovulation, more frequently referred to as intermenstrual or Mittelschmerz's disease.
3. True organic diseases which require surgical care.

It is the first two groups I wish to discuss first, in order to emphasize their importance in making differential diagnosis of acute abdominal pain which may necessitate a laparotomy.

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Conversion symptoms, the emotional or psychogenic cause of abdominal pain, are the type most frequently overlooked. This is apparently due to the fact that most surgeons have been taught that any acute abdominal pain represents true organic disease and therefore necessitates laparotomy. This teaching is not only erroneous, but tragic for the patient who submits to laparotomy because of psychosomatic symptoms. The question is asked: Can true pain exist without some underlying disease condition? Miller[6] states, "May I suggest humbly that pain is what the patient thinks it is and the only clue we have as to whether the patient feels the pain is what the patient says about it."

Bennett and Semrod[1] reported that among 100 patients with psychoneurosis admitted to a university hospital, organic disease, including gastro-intestinal disease, hyperthyroidism, organic cerebral disease, and other diseases of vital importance was diagnosed in 72. One hundred and seventy-nine operations had been performed, at least one-half of them unnecessary. Of these 100 patients, 70 showed satisfactory and lasting improvement under psychotherapeutic treatment. Bennett[2] more recently reviewed the histories of 121 women on whom 205 operations had been performed: 159 major, 84 pelvic, 40 appendectomies, 11 gallbladder, 16 thyroid, 5 postoperative adhesions, 3 kidney operations, 46 minor operations. 12 rectals, 24 on tonsils and nasal sinuses, and one for varicose veins. He stated that it was hard to determine how many of these operations were necessary but in the majority of cases the patient agreed to the operation with the understanding that it would bring relief from nervousness, although the chances are that none of the operations were indicated from that point of view.

The fact that so many patients presenting pain due to psychogenic causes are subjected to unnecessary operations reflects on the teaching, either in medical school or during a residency. Apparently too much emphasis is placed on diagnostic laboratory procedures and too little on clinical evaluation of the history. I am not a psychiatrist and have never had psychiatric training, but I feel that most of us can suspect the presence of a functional disorder merely by allowing the patient to talk and get his history as he presents it without interruption. The history is one means by which psychogenic pain may be suspected and then confirmed or ruled out by a psychiatric consultation.

A number of years ago a physician with whom I was discussing the end results of operations on patients with poor psychiatric backgrounds told me the following incident: A well known surgeon had consented to perform a laparotomy on a patient because she insisted she had a frog in her stomach. At first he tried to dissuade her, but finally he decided to perform the laparotomy and present her with a frog. This was done and the patient was asymptomatic for six months. She then returned and demanded a second laparotomy because of the fact that frog's eggs had been left in her stomach at the time of the original operation. I do not have a further follow-up on this patient, but I do not believe we have to stretch our imagination to guess the end results of such a procedure.

Greenacre reports[3] the following case:

"The patient was seen in the psychiatric out-patient department of the New York Hospital over an 18-month period. She is representative of a group of cases with which we, in a psychiatric clinic of a general hospital, became quite familiar, and I am quite sure it is a group which the medical and surgical physicians also encounter, for patients of this general type come to them first. The patient, a woman of 54, came to us in 1937 with a complaint of pain in the ethmoid region for three years, stomach trouble for ten years, pain across the lower abdomen for two years, and transient sensations of a dead feeling over the back of the head and chest following periods of emotional upset for two years. I am quoting from the patient's own statement of her difficulty and it is noted that her symptoms are all in somatic terms and betray some degree of medical sophistication. She had, in fact, been referred from the medical clinic where she had been considered as predominantly a case of hypochondriasis and this diagnosis seemed borne out by her examination in seven other clinics as well. The number of examinations necessary to arrive at this diagnosis is really impressive.

"Her hospital experience began 32 years ago, when at the age of 22, she had first a dilatation and curettage. This was followed at 24 by a uterine suspension, at 30 there was a right kidney suspension and an appendectomy and later in the same year an ovariectomy, hemorrhoidectomy and another dilatation and curettage at 39. There was a new operative bout, and another suspension of the right kidney and in the same year an operation on the nasal septum. At 40, a complete hysterectomy was followed by peritonitis. At 41-42 a tonsillectomy was done and next a bilateral antratomy which had to be repeated on the right side. At 49, the right kidney was removed and at 52, finally an ethmoidectomy was accomplished. When one looks over this table of operations, it is apparent that they have occurred in general, at four periods in the patient's life; the first at 22-24, the second 30-31, the third 39-40, and the fourth at 49-52. Thus, curiously enough, we note that roughly the patient enters each decade of her life with a surgical initiation; and that the operative work has, as it were, extended itself from below upward, beginning with the genito-urinary system, making a detour into the gastro-intestinal system and finally coming to rest in the naso-pharynx.

"Neither can we now, from behind the screen of these 16 to 17 operations to the lapse of so many years, say much as to the positive indications for the various procedures undertaken. The patient now makes the impression of a morbid willingness to submit to any operative procedure, in the hope of a miraculous relief, which is contrary certainly to all the experience which she has gathered in the past 30-35 years. In other words she now shows an attitude of addiction to surgery, somewhat similar to other forms of addiction."

Wearn[9] in his chairman's address before the Section of Internal Medicine of the American Medical Association in 1947 stated: "Of some 15,000,000 men examined by Selective Service, 1,875,000 were rejected on the ground of neuropsychiatric disorders. This represents 37 per cent of the men rejected for all causes; and even after this initial

screening, 39 per cent of all medical discharges from the army between January, 1942, and December, 1945, were classified as psychoneurosis. At least 5 out of every 10 patients who consult physicians today prove through examination to have no organic basis for their complaints."

Acute abdominal pain is frequently caused by painful ovulation which is not recognized by the surgeon or by the attending physician. It usually occurs in the younger woman in the twenties or early thirties. This condition is also known as intermenstrual pain or Mittelschmerz's disease. A characteristic point in the history is that the pain occurs 10 to 12 days preceding menstruation. There may also be evidence of scant vaginal bleeding at that time.

This condition has been known for over a century, as Pouchet in 1847 discussed it in a book on ovulation and conception in mammals. Sir William Priestly in 1782, Howard Kelly of the United States, and Mittelschmerz in Germany discussed the condition frequently. The diagnosis should not be difficult if we keep the possibility in mind and elicit a careful history. Many a patient will volunteer the information that the pain occurs 10-12 days preceding menstruation and occurs with great regularity. There are no constant pathologic findings in intermenstrual pain either microscopically or macroscopically. There is no unusual thickening of the ovarian capsule which has been suggested as a possible cause of pain. The physiologic nature of the disorder does not interfere with reproduction and is never a cause of sterility. The pain is not of a permanent nature, and in many cases may disappear without any form of treatment.

There is real danger of abdominal hemorrhage resulting from a ruptured graafian follicle or corpus luteum cyst. The hemorrhage may be quite profuse in the peritoneal cavity and in its presence there may be difficulty in ruling out ruptured ectopic pregnancy, a diagnosis that is frequently made by error. A laparotomy is indicated in severe hemorrhage from a ruptured cyst as well as in a ruptured ectopic pregnancy. Sackett[7] has reviewed the subject of intraperitoneal hemorrhage of the ovarian origin and his bibliography is most exhaustive on this type of hemorrhage. In the majority of hemorrhages from a graafian follicle or corpus luteum cyst there is no free bleeding in the peritoneal cavity; if present, it is minimal in amount. The pain is caused by distention of the follicle or cyst.

The treatment of intermenstrual pain is to avoid a laparotomy in the absence of profuse bleeding in the peritoneal cavity, and these constitute by far the majority of cases. There is no specific medication or treatment for recurrent attacks of pain except rest. The patient usually finds that by resting in bed for one to two days she can greatly diminish the severity of the pain which then spontaneously disappears and never returns.

Follow-up observations on the results of laparotomies performed for psychogenic causes or intermenstrual pain show that the procedure is unsatisfactory and frequently harmful. Some patients may have eight or ten laparotomies and often become addicted to the use of morphine. Others may develop intestinal obstructions which will necessitate one or more operations for correction, and fatalities do occur in these cases.

The true organic lesions causing acute abdominal pain in their order of frequency are: acute appendicitis, intestinal obstruction, whether from neoplasm of the large intestine, intussusception, volvulus or mechanical obstruction of the small gut from bands or adhesions; perforated ulcer of the stomach or duodenum; acute cholecystitis; torsion of ovarian cyst or pedunculated fibroid; torsion of the omentum; and rupture of viscera due to trauma of abdomen.

In these conditions the diagnosis needs no detailed discussion, as the symptoms, physical findings, and laboratory findings are well known to both the internist and the surgeon. Treatment is usually surgical operation either during the acute stage or as an elective procedure. If an operation is to be performed during the acute stage the patient should be well hydrated before laparotomy is done. If the patient has been ill for 48, 72, or 96 hours from peritonitis it may be better to delay the operation for 12 to 24 hours so that a fluid balance can be established; and of course chemotherapy is instituted immediately.

Cases of acute intestinal obstruction should receive special mention in view of the rather general use of the Miller-Abbott tube. I refer to obstructions of the mechanical nature, not obstructions of the adynamic or paralytic type. From my observations at Bellevue Hospital, which has an active ambulance service, tumor of the large intestine and strangulated hernia are the most frequent cause of mechanical intestinal obstruction. The treatment of the latter is obvious and an operation should be performed as soon as hydration permits. Unfortunately patients with tumor of the large intestine causing complete obstruction have been and still are being treated with a Miller-Abbott tube for decompression purposes. This practice should be completely condemned. There is no place for the Miller-Abbott tube in the management of obstruction of the large intestine. Surgical decompression is required in these cases as soon as the general condition of the patient will permit. In the treatment of complete obstruction of the small intestine the Miller-Abbott tube should be condemned. This is also a surgical problem and should be so handled.

The Miller-Abbott tube does have a therapeutic place in cases in which partial obstruction has developed following recent laparotomy. Fresh adhesions may not need a second laparotomy if the intestine can be kept decompressed for several days. The Miller-Abbott tube has a place also in the treatment of adynamic or paralytic ileus.

I should like to mention briefly the significance of abdominal pain due to femoral or inguinal hernia. A small hernia may cause partial or complete obstruction of the small intestine. The hernia may be so small that it is overlooked on physical examination and is not suspected as being the cause of the abdominal pain. A typical patient with such a condition is an emaciated female between the ages of 60 and 80.

Retroperitoneal hemorrhage resulting from trauma may produce severe abdominal pain and clinically an associated paralytic ileus may be present. The retroperitoneal hemorrhage may or may not be associated with rupture of the kidney. In reviewing the traumatic injuries at Bellevue Hospital on two occasions,[4,5] I have been impressed by the number of patients who presented a typical picture of acute "surgical" abdomen although the symptoms resulted from hemorrhage outside the peritoneal cavity associated with reflex ileus. This condition should be suspected if the injury has been over the lumbar region, and there may be evidence of abrasions, ecchymosis, or swelling. Occasionally there may be associated fracture of the transverse process of one of the lumbar vertebrae. The history and physical findings are most important in making a differential diagnosis in this condition. Flat roentgenograms of the abdomen may be misleading as they may indicate fluid levels and cause us to suspect a true organic obstruction, when in reality the cause is a functional disorder of the gastro-intestinal tract and does not necessitate laparotomy.

SUMMARY

Acute abdominal pain can be more accurately interpreted by eliciting a careful history and studying the physical findings than by any other means. The results of laboratory and x-ray studies are frequently misleading and too great reliance should not be placed upon them in evaluating the indications for laparotomy.

The consultant should be given the opportunity to obtain the history directly from the patient. Thus he can better evaluate the symptoms since he is studying an individual and not a case report.

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The Nervous Woman in Industry

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FOR the purpose of this presentation, a nervous woman is defined as that woman who finds her general well-being impaired because of a state of tension produced by inability to cope satisfactorily with certain conditions or circumstances.

Such a woman is a source of concern to herself since she is unhappy, often frightened of her condition, and, at least in her own mind, frequently ill. She is a source of concern to her employer as her work efficiency is decreased and her absenteeism increased. She is a source of concern to her physician because of the persistency, chronicity, and variety of her complaints.

SOURCE OF MATERIAL

In an attempt to find the underlying causes of nervousness of women in industry, the medical department of a large industrial concern analyzed histories of 25 nervous women over a three-month period. This is not a large series but is assumed representative of the problem, and the data are fortified by years of experience in meeting patients of this type. The medical department referred to is composed of physicians in private practice who spend only part time in industrial practice. As they are not trained in psychiatry or psychology, these observations and conclusions are not those of specialists in these fields.

The business concern here considered does not have hospital or sickness insurance in the usual sense of the term. It does have a sickness disability benefit plan which, after two or more years of employment, provides full or partial pay to employees absent because of sickness. The duration of payments is on a sliding scale and ranges from a few weeks for the two-year employee to a full year for a 25-year employee. In ten of the 25 cases reviewed the employees were declared unable to work by a physician. These women were therefore drawing sickness benefit payments. These ten cases reviewed in a three-month period represented 1,361 days lost from work and $9,580 spent in sickness benefits. The figures are indicative of the loss of time and the cost of disability of this type.

The patients came to the medical department voluntarily, or were referred by a supervisor who noted a health problem, or were interviewed at the request of a company department for determination as to whether or not they were able to return to work.

As the medical department acts only in an advisory capacity, its members were able to observe the methods used by other physicians in management of these nervous patients.

It early became apparent that these women were unable to adapt or adjust themselves to a variety of circumstances, and therefore they will be called "maladjusted." Their complaints were numerous as may be noted in Table 1.

TABLE 1.—*Nature of Complaints Among 25 Nervous Women in Industry*

Complaint	No. of Cases
Nervousness	16
Insomnia	12
Weeping	11
Tachycardia	3
Tremor of Fingers	3
Abdominal Pains	3
Hot Flashes	3
Headaches	3
Dizziness	2
Smothering Sensations	2
Weakness	2
Nauseau	1
Pains in Joints	1
Pains in Neck	1
Pains in Arm	1
Poor Vision	1
Generalized Itching	1
Inability to Decide	1
Hair Falling	1

Nearly every patient presented two if not all three of the main complaints—nervousness, insomnia, and weeping. Once a patient was recognized as probably being in the group of nervous women, an examination was done to determine the presence or absence of organic disease. (Most of them had psychosomatic disease or coincidental organic disease, but only four had active organic disease.) Then an effort was made to discover what were the maladjustment problems. This was in some patients easy, in others most difficult. The best method seemed to be to ask, "Are you happy?" and to watch the reactions. If the answer was negative, the story was easily obtained. Or if affirmative, but associated with hesitancy or vagueness plus moist eyes or actual tears, other key questions such as "Are you happily married?" Do you have any financial worries?" "Are you homesick?" "Do you like your work?" usually elicited the story.

Occasionally a patient will present to the medical department a letter from a doctor to the effect that the patient's work is so nerve-wracking or exhausting that the patient needs a six-month rest. It is true that for physical or temperamental reasons certain types of work may not fit the employee. However, this is usually noted early in employment and a suit-

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able adjustment made. It is rare to find in the case of an employee with relatively long service that the nature of work is at fault. Usually it is found that the employee herself is at fault and has blamed her job unjustly or is hiding another reason for maladjustment. Substantiation for that conclusion is drawn from the fact that in this series there were patients from each of the various kinds of jobs within the company.

As to age of patients, six were in the 15-25 age bracket, four were between 25 and 35, nine between 35 and 45 and six between 45 and 55.

Among the 25 women in this series, those who had been with the firm the shortest time predominated. Eight had been in the company's employ less than five years, four between five and ten years, two between 10 and 15 years, four 15 to 20 years, five 20 to 25 years, and two 25 to 30 years. Eight had severe marital troubles, eight were happily married and nine were single. Most of the women had a high school education or better, seven had had pelvic operations, five had grown up in disturbed home environment.

CASES

In an attempt to condense the various problems of these women and to classify their maladjustments, it was noted that a very important group might be called the "anti-socials." These women were of various ages. They had really never had pleasant relationships with their fellow humans. Some were not able to live harmoniously with their families and had left home as soon as the law permitted. Many had been married and divorced. One had been married and divorced three times. Nearly all lived alone and had few friends, little recreation, and no hobbies. Work was tolerated but many criticisms were directed toward fellow workers and superiors. In brief, these people were unable to get along with anything on two legs. They were all lonely, all overly critical and without realizing it were all thirsty for a companionship that they made no effort to encourage. Seven of the 25 belonged to this group.

Four of the women were classified in the so-called "exhausted state" group. These women for the most part had a heavy burden of outside work, principally housekeeping. The woman in this bracket works eight hours, then goes home to cooking, dishes, and other household chores. On week-ends the husband has a change from the office to, say, a garden; but the wife spends more time in the same old house with more chores. After years of this, she is finally exhausted. Why did she continue working year after year? Usually to gain financially, to own a home, and to enjoy the luxuries an extra pay check represents. Also in this group is the employee who has to care for a sick relative, usually an unmarried daughter caring for a sick or senile mother.

Two of the women in this series were disappointed in love. One young woman experienced smothering sensations dating from the time her boy friend suddenly married a rival. The other, an older woman, could not forget or forgive her husband who had run away with another woman ten years before. Telling of the episode still brought an emotional outburst.

Four were homesick. One of this group found it difficult to adjust to marriage and her first job as well as to leaving home and mother a few thousand miles away. One young woman had left Ireland a few months previously to be in this country with a relative. She disliked the United States, California, San Francisco, the company, and her work. Only the fact that she considered Ireland such a wonderful spot indicated she was not of the "anti-social" group.

Four of the women were not adjusted to their work. It was felt by the examiners, however, that the work was not primarily responsible but that the individual was at fault in not being able to adjust to conditions easily met by others. One woman just starting employment found it difficult to adjust her sleeping and eating habits to evening hours. Another woman feared she might lose her position at a time of great financial strain and as a result had smothering sensations. Another felt she was unable to make decisions. The fourth was upset because in transferring to the West Coast from the East she had given up a supervisory job. "It is much better to give orders than to get them," was her comment.

Four of the women in the series had active organic disease which either played a major role in the maladjustment or confused the picture. One woman who had given two blood transfusions had marked secondary anemia. Rather than weakness and fatigue, the symptoms in her case were insomnia and weeping. In one woman a surgical operation had caused the menopause. Another patient had dysmenorrhea that resisted all treatment and was a source of torment and inconvenience. In another case the presence of a toxic thyroid adenoma hid the real issue. The patient was first seen in 1939 with a clinically toxic thyroid adenoma. It was removed surgically and histologically proved toxic. However, the patient continued to be extremely nervous for several months. It was discovered she was hypothyroid, and there was slow improvement on thyroid medication. Later, however, she became quite agitated, was unable to sleep, and cried easily. In spite of a basal metabolism of −17 per cent and the discontinuance of thyroid medication she continued to be quite nervous. As it was at this time that case histories for this presentation were being obtained, the patient was questioned and it was found that her original trouble started in 1939 at the death of her mother. The patient then had been upset for a prolonged period. Her recent distress was associated with the recognition by her that she had for 13 years been in love with a married man and therefore could not have a home and family which she had dreamed of as a younger girl. At the same time she had been a participant in litigation over an estate. Moreover, she had been living in a five-room house with four adults and had no

privacy or quiet. It was felt by the examiners that the thyroid condition was coincidental and that the basic cause for upset was emotional conflicts.

TREATMENT

In the treatment of these nervous women it must be remembered that the practitioner who has dug out the story of trouble has usually gained the patient's confidence and friendship. Frequent discussions and advice are often necessary. In severe cases or those cases that suggest psychopathic tendencies, psychiatric treatment is of great help.

However, it is not unusual at the mention of a psychiatrist to have the patient reply, "Oh, doctor, I have felt I might be going crazy and now you must think I am, too, because you have asked me to see one of those doctors." Another bar to psychiatric treatment is that many of these women have limited incomes. Part-pay clinics try hard, but our experience has been that they are overcrowded and that personnel changes are so frequent that a patient acquainted with one doctor often has a relapse because she must become acquainted all over again with another. Other persons of great assistance are the company welfare workers, who can cooperate with the doctor in advising and guiding the patient.

Such patients recognize that their work is poorly done, and that is an added cause of anxiety. Few of the patients were benefited by rest alone, but as an escape from work, rest is important. At times a change of environment is most beneficial.

It is quite surprising that there exists such a fear of sedatives in the minds of both patient and physician. Perhaps the lay press has been responsible. We have in fact found the use of small doses of sedatives in the daytime and hypnotics at night to be of great benefit. If the patients can "let down" and can escape the depressing thoughts associated with a wakeful night, a great stride is made toward relief. Risk of addiction or overdosage could be greatly lessened by prescribing small amounts of sedatives at a time, giving definite instructions as to use, and refusing telephoned requests from a pharmacist for permission to refill a prescription.

Excessive use of stimulants is a factor to be considered. In the present series, only two patients used tobacco or coffee to excess. However, one woman not in this series, who had been under treatment for a considerable period because of nervousness, had never been asked and had never volunteered that she smoked up to three packages of cigarets and drank ten to fifteen cups of coffee a day. Excessive use of stimulants is a handicap to the correction of nervousness and should be avoided.

With the exception of the patient with surgically induced menopause, no one in our series found the physiological menopause a primary major upsetting factor although nervous conditions existed coincidentally with the physiological menopause, and in some of the women nervousness was aggravated at the time. Several patients who were given hormone substances, usually by injection, over a period of months or years experienced only moderate decrease in nervousness or no relief at all. The physiological menopause need not cause distressing symptoms. When it does, proper therapy over a reasonable period of time should be effective. If the symptoms are not altered, the case should be re-evaluated, as there are probably other contributing factors.

Attention to general hygiene is an old dictum. It is surprising the number of young women who stay up nights and average only five to six hours of sleep when they should have eight or more. Older women with demanding duties at home may average only a few hours of sleep. Anyone suffering from lack of sleep is potentially a nervous person. To inquire into eating habits may seem foolish, yet one weeping girl (not in this series) had spent so much for clothes that she found it necessary to curtail outlay for food to the point that her daily intake of calories was only 400 to 500. Some of the patients need recreational advice; the need for fun, for companionship poses a serious problem in the lives of many.

PROGNOSIS

In cases in which the nervousness is caused by simple problems and is of recent origin, patients usually can be entirely cured. Optimism is justified if the patient's attendance and attitude record is good and home conditions are favorable. On the other hand, if these are not satisfactory, the outlook is pessimistic. In older people, and particularly in the so-called "anti-social" group, the condition often is irreversible.

CONCLUSIONS

The "nervous woman" in industry usually is maladjusted. Questioning by a physician often will elicit the underlying cause. Sound advice then may restore to fuller usefulness the unhappy person who is a poor worker, a chronic complainer, and a drain on sickness insurance.

2000 Van Ness Avenue.

At the Head of the Table

WESLEY BOURNE, *Montreal*

Nec solum gens illa sua contenta salute
Excubat hospitibus, contraque nocentia monstra
Psyllus adest populis. LUCAN, IX. 909*

IN the fourth century there lived at Cyrene "a man of many and wandering thoughts" (Mrs. Browning), Synesius by name. Among his writings is a book called *Praise of Baldness*. He reflects that hair is the mark of the beast, that man is in the main bald and that with dogs, the more hair, the less sense. "So the balder a man is, the wiser and the more divine we may take him to be. Hair like the adornment of growing corn withers when the fruit, here the brain, is ripe. Of all shapes the sphere is most perfect—and that is the shape of the bald head," (T. R. Glover's *Life and Letters in the Fourth Century)*. Our head is our most heavenward part. The best of men, priest and philosophers, are all painted as bald. Synesius hoped that the "lovers of hair" (Φιλόκομοι) would be ashamed and adopt the reasonable and honorable practice of shaving, but always pay special honor to those who do not need the barber. This allusion, although rather facetious, is not entirely inapposite to the thought implied by the title of this paper, as it not only draws attention to the relative importance of the human head, but also refers to what goes on within the calvarium of him who officiates at the head of the operating table.

In further simile, witness the influences of the myriad and multiform functionings as they play one upon another, now controlling, now being affected; almost assuring a beauty behind all phenomena; active through them, immanent, beneficent. A good example comes from the recent work of Smith,[8] showing the presence in the cat, dog, and monkey of cortical areas possessing similar cytoarchitectural structure and yielding physiological responses, which presence suggests the existence of a fundamental plan for the cortical control of respiration in the general scheme of cerebral cortical evolution. This observation has been confirmed, indeed, extended by Bailey and Sweet,[1] division of neurology and neurosurgery, University of Chicago Clinics, in their statement that from the orbital surface of the frontal lobe an area in the gyrus orbitalis near the olfactory tract was found to give rise, upon stimulation, to inhibition of respiration, rise of blood pressure and decrease in the tonus of gastric musculature. May these apogean similitudes, in fancy, be given the anesthetist as he uses his senses in endeavor to guide the one who suffers.

We must remember that this quality of keeping watchful guard over the patient has not been acquired exclusively by the anesthetist. He has, in truth, inherited it with gratitude from his predecessors in medicine generally the world about, of whom there are no better examples than the founders of the hospitals, and the medical schools, societies and journals of this your Golden State. Immortal in California medicine[5,6,7] are such names as Father Junipero Serra and Dr. Pedro Prat, pioneers of the eighteenth century; Dr. Richard Den, who answered the layman's question, "What is Mrs. So-and-so's ailment?" with the simple parry, "sickness"; Elias S. Cooper, the founder, in 1858, of the medical department of the University of the Pacific, which in 1908 became the School of Medicine of Stanford University; Hugh H. Toland, founder, in 1864, of the Toland Medical College, which became the Medical School of the University of California; Levi Cooper Lane, who established the library which still bears his name; and Joseph P. Widney, the great educationalist, who incepted, in 1885, the Medical School of the University of Southern California, one of whose deans, Walter J. Barlow, gave the library which bears his name. There are many other exemplars, revered equally by the general practitioner and the specialist.

The epigraph of this essay is taken from Lucanus and would seem not too inappropriately placed as it implies that we belong to a group of individuals who unselfishly keep guard over those who suffer. It draws attention to the exercise of thought and, as well, to the doing of deeds by the anesthetist in the interest of the patient. "At the head of the table" an anesthetist uses his senses momentarily on behalf of the one who is receiving surgical attention. George Malcolm Stratton,[9] professor of psychology in the University of California, from his translation of *Theophrastus on the Senses*, shows that this Greek author pointed out that when the senses are functioning properly, they lead to truth, and that "In the usual course of things perception is 'in accord with nature'; like the knowledge process generally, it is naturally aligned with what is better, working to our advantage, rather than to our confusion and loss." Pascal wrote that "Man is obviously made to think. It is his whole dignity and his whole merit; and his whole duty is to think as he ought."

L'homme est visiblement fait pour penser. C'est toute sa dignité et tout son merite, et tout son devoir est de penser comme il faut.
Les Pensées de BLAISE PASCAL (1623-1662).

Presented before the Second General Meeting of the 77th Annual Session of the California Medical Association, San Francisco, April 11-14, 1948.

Chairman, Department of Anesthesia, McGill University.

*Translation: And that group of persons, not satisfied with safety for themselves, keep guard over sufferers and aid mankind against deadly monsters.

Let us from such *lessons seek and find instruction with an humble mind* (Southey, *His Books)*. Let us envisage a hospital with a department of anesthesia whose personnel is composed of graduates in medicine. Let us visualize these as organized, not only to give service as anesthetists, but also to provide opportunity for the young doctor who desires to learn the subject, so to specialize. There are, already, several such centers of learning and (happily) their numbers are steadily increasing. Of the "voice" of any one of some of these, we may say, in words like those of Sir Arthur Quiller-Couch *(Studies in Literature: The Commerce of Thought, VIII)*, "The fame of it spreads almost as pollen is wafted on the wind: but spreads, and alights, and fertilizes." For a sectional meeting of anesthetists in Kingston, Ontario, I[2] described the three-year diploma course in anesthesia presently functioning in the Department of Anesthesia at McGill University. Let me quote one part of that description:

"In this course the aspirant must have had one year of internship in an approved hospital, preferably in the department of internal medicine. Throughout the three years, the candidate resides in one of six hospitals, moving from one to another every six months. In this rotative manner the individual gains a diversity of experience under the tutelage of many qualified anesthetists. The benefits of this many-sided method of acquiring skill are readily evident, for he who learns from many masters is bound to be more versatile, more Jeffersonian and more percipient than he who ranges under one rubric."

He, who at the head of the table, from an anesthesiological point of view, regulates the state of affairs inobtrusively and in concord with the surgeon, has two main duties to perform: firstly, the conduct of all that has to do with the anesthesia; and secondly, the guidance of those who are in assistance and are there to learn anesthesia. These two offices are fulfilled virtually the one with the other. For example, in a given case, with the pains of taking care to be prepared for eventualities, explanations are given for all that is done. During the operation, the procedure is considered and the occurrences discussed, in soft voice not to distract those at the rest of the table. In the postoperative period, similar vigilant attention is paid to the carrying out of both of these two intensely interesting obligations. Thus may young men learn anesthesia as they help in no small degree. They may say of themselves, with Wordsworth,

> *That we can feed this mind of ours*
> *In a wise passiveness.*
> *Think you, 'mid all this mighty sum*
> *Of things for ever speaking,*
> *That nothing of itself will come,*
> *But we must still be seeking?*
>
> EXPOSTULATION AND REPLY

In the realm of anesthesia, art will little wane, nor will science long lag. Never shall either take to bed, and expire, and be beatified; indeed, never even be

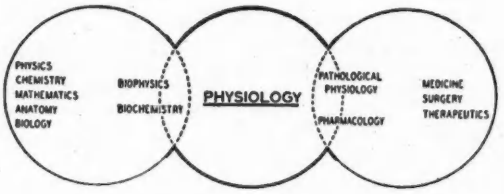

Figure 1

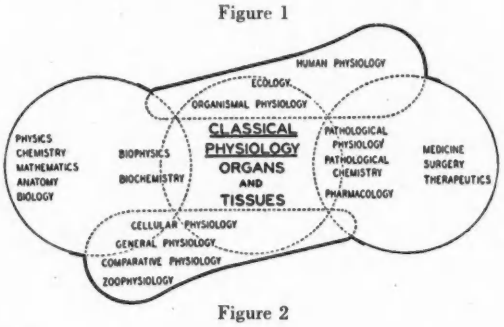

Figure 2

faded, jejune, effete; never, as long as there is confluence of deep thought among young men, in laboratory and in clinic, to face and to solve perplexities; to find and to tap wells more and more abundant, fresh and pure. And, the sources of knowledge are many as they extend to our specialty. One is not long "at the head of the table" before he is convinced of the importance of being familiar with the *classical physiology of organs and tissues* as it still remains squarely in the middle of the picture drawn by Eugene M. Landis,[4] of Harvard University, and reproduced here in Figures 1 and 2 (permission gratefully acknowledged). "This [*classical physiology*] blends in one direction with cellular, general, and comparative physiology, all leaning towards physics, chemistry and biology. At the other end of the scale organismal physiology, ecology and human physiology lean toward pathological physiology and medicine, from which, in fact, many of the truly organismal problems and quantitative studies on man have originated." When we consider that "this multiplicity of subspecialties is a stimulus, an opportunity and a burden, all at the same time," that is, to the physiologist, we should spare no effort in associating ourselves with and learning from him as well as the anatomist, the biochemist, the biophysicist, the pathologist, and the pharmacologist. Also, in practical manner, we should encourage *apt* young physician-anesthetists to become skilled at research and proficient at teaching. Everybody knows that there is at present a direful dearth of anesthetists, and you and I know that many a center is in need of someone capable of guiding a department of anesthesia with regard to the best interest of the patient, the training of personnel and the carrying out of investigation.

And now, speaking of research, we may be assured that there will always be frontiers for inquiry in anesthesia, frontiers wide and deep, to be pierced

following progress in the basic sciences. During the past 15 years especially we have witnessed tremendous advancement in our knowledge of the chemistry and physical chemistry of body processes. We have long known that the remarkable chemical reactions in the cell are brought about by catalysts or enzymes which are capable of accomplishing almost instantaneously feats of synthesis and degradation in an aqueous medium and at 37° C. which in the laboratory cannot be achieved except by prolonged chemical procedures requiring high temperatures and drastic treatment with harsh reagents. It is only recently, however, that the vast accumulation of information concerning these enzyme-catalyzed reactions has been integrated into a coherent science of enzymology. When we consider that each cell contains an array of enzymes which operate side by side and in close coordination, simultaneously building up and breaking down dozens of complex products of metabolism, we can appreciate the delicacy of the equilibrium within the cell and the complex physiological equilibrium between all the cells of the body. Too few of us appreciate how sensitive the cellular enzymes are to disturbances in the composition of the cellular fluid. Very slight changes in the content of water, electrolyte, or metabolites, or the presence of foreign substances may seriously disturb the cellular enzymes. Thus, what we call health is fundamentally a chemical and physiological equilibrium. We all know the severe repercussions of water or salt depletion, malnutrition, hypoxia, renal impairment and so forth, but we seldom think of these diseases in terms of disturbed enzyme function. The action of drugs and the phenomenon of poisoning also are simple manifestations of the interference with normal enzyme activity. When the disturbance becomes severe or prolonged, the damage may be irreparable. The recovery of the patient depends on the restoration of the normal chemical composition of the cell fluids and the recovery of normal enzyme function.*

In the light of these basic considerations, the mechanism of the processes of disease becomes more intelligible. Furthermore, we appreciate how important it is to use drugs with the greatest possible discretion and always to be mindful of the importance of adequate nutrition, of oxygen supply and of the maintenance of salt and water balance.

We learn, too, that the distribution of enzymes in all organisms, be they plant or animal, ameboid or human, is gene-controlled and subject to the laws of heredity. Now and then we meet with an individual who apparently enjoys good health, but who throughout life excretes pentose sugar in the urine, or may excrete phenyl pyruvic acid as a result of some aberration in the metabolism of tyrosine or phenyl alanine. Again, the cells of the black areas of the skin of an animal contain certain enzymes which are capable of producing the black pigment melanin, whereas these enzymes are lacking in the cells of the white areas. Whether certain abnormalities we meet with are caused by the complete lack of one or more enzymes, or a partial lack, or a lack of the enzymes in a specific tissue, remains to be elucidated. Following the same line of observation, we know that individuals by inheritance may possess a predisposition to certain types of failure, or, on the contrary, an exceptional degree of resistance and stability. A knowledge of the individual's family tree is all to the good at any time but is especially important in the field of preventive medicine which is concerned with keeping people well.

The nutritional status of the patient is another consideration that has come to the fore since the days of the late war. Although previously known, it has not been given much attention that the undernourished patient is a relatively poor surgical risk and that the patient in good nutritional condition not only withstands trauma better but makes a smoother and more rapid recovery afterward. It is common knowledge also that the undernourished patient is more liable to liver damage following surgical operation and from drugs. We now realize that in the past we have paid too little attention to the caloric and other nutritional requirements of the patient. We are aware, too, that it is practically impossible to restore the chronically undernourished individual to normal within a short time simply by correcting his nutrition. In future the nutrition of the patient doubtless will be a matter of primary concern.

From the realm of chemistry and pharmacology, the anesthetist can expect an ever increasing number of new agents. While the relationship between chemical structure and biological activity is still obscure, the astounding progress of recent years in the field of synthetic chemistry augurs well for new fundamental advances in our understanding of the action of specific chemical groups or structures on enzyme activity of the cell. Whatever advances may be made in the realm of pharmacology, one should still feel that any biologically active agent ought to be used with discretion. As a general rule the use of any drug should not be expected to correct the basic cause of the disturbance.

Plutarch, the sage of Chaeronea, points out that geographers used to thrust into the extremities of their maps those countries that were unknown to them, remarking at the same time, that all beyond is hills of sand, and haunts of wild beasts, frozen seas, marshes, and mountains that are inaccessible to human courage or industry. This hypothetical method of reasoning may not now be allowed with the dispersing of hyperborean cloud by scientific advances. The anethesiologist will always be interested in the progress of the fundamental sciences, indeed, may often collaborate. Similarly, too, he will keep himself acquainted with all else that goes on in the whole of classical physiology. Has he not turned his attention with enthusiasm to the works of Knisely, Block, Eliot and Warner[3] on *Sludged Blood?* These observers have defined certain prop-

*I am deeply indebted to Orville F. Denstedt, Associate Professor of Biochemistry at McGill University, for guidance in these remarks.

erties of normal blood, of blood flow, and of the vessel walls; have given evidence that these properties are necessary for the functioning of the circulatory system; have described visible responses of the vascular system and/or blood to specific stimuli; have described visible pathological structures and processes; and have set resultant goals for therapeutics. The articles of these investigators are well worth studying inasmuch as they summarize, in part, that their observations, experiments, and deductions supply evidence that the undispersed blood cells provide a common, easily understandable set of factors whereby many diseases can and do damage the bodies of lower animals and of man. They express the hope that as we learn how to keep blood fluid and from becoming agglutinated, or should we say, aggregated, how to keep the vessel walls intact, the red cells from being destroyed, and blood volume adequate; many effects of other pathological mechanisms, in the authors' words, "will stand out clearly, unobscured by the sludge mechanisms. Each will, of course, then receive the undivided attention it merits. The sludges are now ready for study by all the intensive investigative methods our age affords."

The mind of the anesthetist grows accustomed to dwell upon such subjects as I have tried to portray, even, at times, when not at the head of the table. To be sure, I might multiply them and you will agree that they are inextricably intertwined. With training, as time goes on, there comes to the anesthetist, in distinct human manner, the power to see and to know, to feel spontaneously and to think with understanding. He will attain the ἡ ἀθαυμαστία attitude of philosophers, that is, of not wondering at anything; will attain *divine tranquility* which Tennyson defines so well. He might be likened to Louis de Bourbon in the words of Bossuet:

> *Ses partis lui rapportent jusqu'aux moindres choses: on l'éveille à chaque moment; car il tenait encore pour maxime, qu'un habile capitaine peut bien être vaincu, mais qu'il ne lui est pas permis d'être surpris.*
>
> ORAISON FUNEBRE.
> Prononcée dans l'église de Notre Dame de Paris le 10 Mars 1687.

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The Laboratory in the Diagnosis of Communicable Diseases

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MANY of the communicable diseases that formerly constituted a significant proportion of the medical practice of physicians have become all but extinct. Some of these, such as typhoid fever, are so infrequent as to be seen rarely, if at all, in the practice of most physicians. Numerous other communicable diseases occur so infrequently that the specific laboratory procedures available to assist the physician in the diagnosis of these conditions are not generally known. The rarity of these diseases makes their recognition by the physician all the more difficult. Moreover, only recently have specific laboratory procedures been developed to assist the physician in making a definitive diagnosis in a number of communicable diseases, particularly those caused by viral and rickettsial agents.

The cases reported in California during the past five years of certain of the communicable diseases in which specific laboratory procedures are available to assist the physician in diagnosis are given in Table 1. It will be noted that a number of these diseases are reported infrequently. We have no way of knowing how many diagnosed cases are not reported or how many cases occur that are not recognized. In addition, in some instances, such as "Q" fever, the diseases have not been made reportable and our only evidence of frequency of occurrence is acquired by specific epidemiological investigation. Several diseases of frequent occurrence are also listed because they still present practical problems in specific diagnosis in which the laboratory can be of assistance.

TABLE 1.—*Cases of Certain Diseases Reported in California During the Five Year Period 1943-1947.*

Diseases	Cases
Typhoid fever	879
Paratyphoid fever—Total	400
A	35
B	305
C	52*
Type unknown	8
Dysentery, bacillary	1,669
Brucellosis	1,391
Plague	3
Relapsing fever	60
Tularemia	36
Influenza	31,877
Infectious pneumonia	16,208†
Rocky Mountain spotted fever	9
Typhus fever	228
Q fever	178‡
Lymphogranuloma venereum	1,063
Psittacosis	26
Encephalitis:	
Total cases reported	828
Western equine (+ Lab.)	59
St. Louis (+ Lab.)	33
Mump encephalitis (+ Lab.)	9§

*Made reportable July 1, 1946.

†Including atypical and virus pneumonia.

‡Not reportable. Cases found in epidemiological investigations to March 1, 1948.

§Laboratory procedure started July 1, 1946.

The following report deals with the laboratory only as it applies to the identification of the specific infectious agent either by isolation and study of the agent itself, or by the demonstration of the appearance of specific antibodies in the blood serum of the host. The commonly used clinical laboratory procedures, such as blood counts, are not considered in this report.

Several recent outbreaks of some of these communicable diseases have revealed a lack of understanding by the practicing physician of the bacteriological and serological laboratory aids that are available. In several instances there has been an undue delay in the diagnosis of diseases through failure to utilize these available services. Some of the more practical laboratory aids will be itemized herein. This is mostly a review of well-known procedures, but experience in the state laboratory has revealed the need for periodic restatement of the more important procedures. In addition, some of the newer procedures in the viral and rickettsial disease field will also be briefly mentioned, together with an indication as to how these services may be secured.

Read before the Sections on Public Health and General Practice at the 77th Annual Session of the California Medical Association in San Francisco, April 11-14, 1948.

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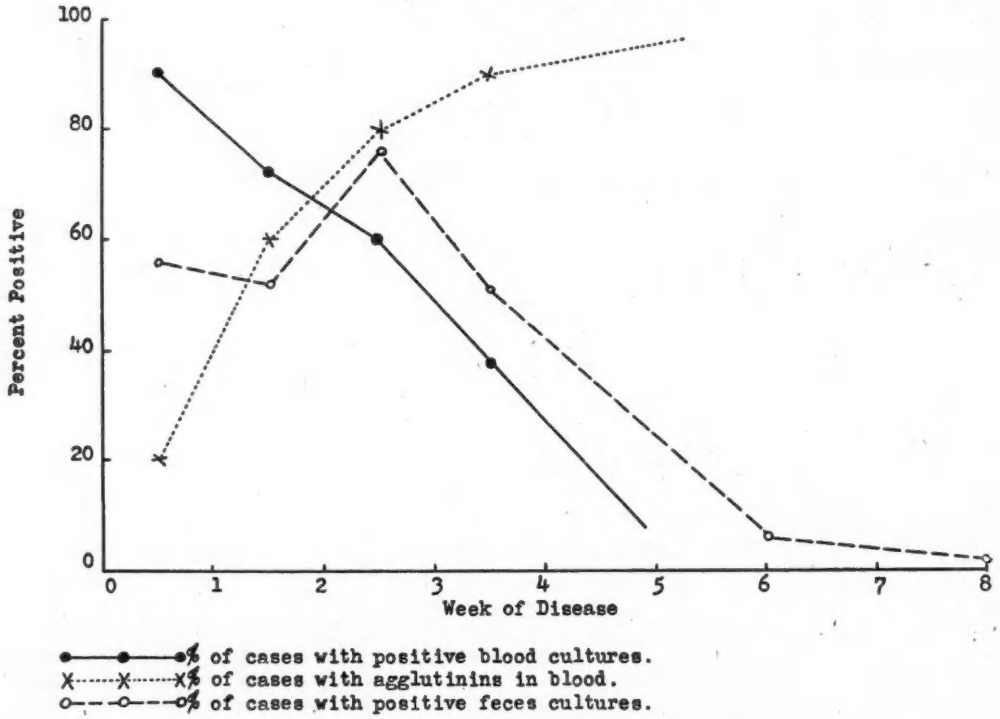
TYPHOID AND OTHER ENTERIC FEVERS

Reference to Table 1 will indicate that typhoid fever has become an infrequent disease. During the past five years, only 879 cases have been recorded in California. Physicians may practice for years, or even a lifetime, without encountering a case of typhoid. This results in a low index of suspicion which in turn not infrequently results in a considerable delay in arriving at a diagnosis. In one recent outbreak, involving 21 cases, the onset of the first case was July 3, yet the first case was not diagnosed until July 25, some 22 days later.[2]

In typhoid fever there are three specific laboratory procedures available to physicians. The first is the blood culture, which, as indicated in Chart 1, may be expected to be positive in upwards of 85 per cent of cases during the first week of illness. The second is stool cultures in which the percentage of cases yielding positive cultures progressively increases during the first two weeks of illness. During the first week, however, stool cultures are definitely inferior to blood cultures. The third procedure consists of the demonstration of specific agglutinins in the blood serum of the patient. It will be noted that



Source: Adapted from Topley and Wilson (2d Ed.; 1941), Fig. 259, P 1198.

Chart 1.—Relation of Isolation of Organisms from Blood and Feces and Agglutination Titer in Cases of Typhoid Fever.

agglutinins begin to appear by the end of the first week of illness but that it is the third week before the percentage of cases positive equals the percentage that yield positive blood cultures during the first week of illness. This time-relationship between blood culture, stool culture and serum agglutinin is shown in Chart 1.

Culturing the blood for *E. typhosa* is a simple procedure that can be readily done by any clinical, hospital or public health laboratory. However, many hospital and clinical laboratories lack adequate materials for efficient examination. One of the most frequent errors is the securing of too small a quantity of blood. A good rule is to obtain at least 20 cc. for the culture.

The recovering of the organisms from stool specimens is a more exacting procedure, and not infrequently laboratory personnel not accustomed to the preparation and use of differential culture media used for such isolations will fail to achieve recoveries from positive stool specimens. Local and state public health laboratory services, where workers in general have more experience with this specific procedure, are available to physicians, hospitals and clinical laboratories to assist in such studies.

Agglutinin tests can be done in any well established hospital, clinical or public health laboratory. Satisfactory antigen suspensions for such tests are available through commercial supply houses or from the state laboratory. For epidemiological purposes, the State Department of Public Health requires that cultures of all isolations of *E. typhosa* be forwarded to the state laboratory for phage typing. By this procedure it is possible to separate *E. typhosa* into some eight specific types which appear to be characteristic and constant for any given strain of organism.* This procedure is frequently of much value in determining the source of any given outbreak of typhoid.

All that has been said with reference to laboratory procedures designed to specifically identify typhoid infections applies almost equally well to infections with *S. paratyphosa A* and *B*.

It should also be noted that any one of a large group of organisms of the genus Salmonella may be responsible for acute gastro-intestinal infections in man. These are usually diagnosed as food poisoning by the physician. They are, however, true infections; the symptoms, as far as is known, are due to the infection and not from the ingestion of preformed toxins. Blood cultures are usually negative and specific diagnosis usually rests upon recovery of the specific organisms from stool cultures. In severe infections, there is a rise in the agglutinin

*Recent work by Craigie and Felix has justified the expansion of this scheme to approximately 24 types which according to preliminary work permits a specific typing of 95 per cent of all cultures of *E. typhosa*. Heretofore only 70 per cent could be typed.

titer in the blood stream. However, since the infections are frequently of short duration and transitory, agglutinin determinations are usually of no value in establishing a specific diagnosis. The state laboratory maintains a Salmonella Typing Service for specific identification of any cultures of Salmonella that may be isolated from such cases. From such studies, valuable information is being obtained relative to the occurrence and distribution of the various Salmonella species in California.

BACILLARY DYSENTERY

In California, bacillary dysentery is currently more prevalent than is typhoid fever. There have been 1,669 reported cases in the past five years. This certainly represents the minimum number of cases actually occurring. The true number is undoubtedly far above this minimum. In bacillary dysentery, diagnosis from the laboratory standpoint rests upon the isolation of the specific organisms from rectal swab or fresh stool specimen cultures. Such cultures are almost constantly positive during the acute phases of the disease if correct laboratory procedures are employed. Blood cultures are rarely positive and serum agglutinins appear inconstantly. The many serological cross reactions with other groups of organisms makes the serum agglutinin of little value.

Again the state laboratory has established a typing service which is available for specific identification of species of these organisms. Because of the epidemiological importance of knowing the specific species occurring in the state it is requested that all such cultures be transmitted to the state laboratory.

TULAREMIA

Thirty-six cases of tularemia have been reported in California during the past five years. In this disease, blood cultures early in the course of the disease and demonstration of rise in serum agglutinins after the second week are of value in establishing specific diagnosis. Positive cultures may also be obtained directly from lesions or buboes. These laboratory services are available in all well established clinical, hospital and public health laboratories.

PLAGUE

Plague still occurs in California, although rarely. In recent years only the bubonic form has been encountered, three cases having occurred during the past five years. Direct examination of smears prepared from aspirated material from the buboe with the application of special staining techniques usually demonstrates the typical bipolar staining organisms. Confirmation is secured by culture and animal inoculation. Due to the danger of handling these organisms in the laboratory the regulations of the State Board of Public Health require that the physician or laboratory communicate by telephone or wire immediately with the state laboratory for specific instructions in the handling of material from suspected cases of plague.

BRUCELLOSIS

During the past five years, the number of cases of brucellosis reported has varied from 260 to 320 per year with a total of 1,391 cases. Evidence indicates that this is probably much below the actual occurrence. The laboratory not infrequently provides all too little aid to physicians in the diagnosis of this disease. The only completely definitive laboratory procedure is the isolation of the specific organism from the blood. Of almost equal significance is the demonstration of rise of serum agglutinin titer during the course of the disease, provided there has been neither administration of vaccine nor performance of skin tests. Either of the latter procedures invalidates the results of serum agglutinin tests. In this disease, repeated blood cultures should be made and repeated agglutinin tests performed. The latter are frequently negative during the quiescent stages of the infection only to become positive during acute exacerbations of the disease. Such a rising agglutinin titer provides good evidence of infection, provided, again, there have been no skin tests nor vaccine administration. In this as in other diseases it should be recognized that the presence of serum agglutinins does not necessarily mean current infection. It means either current or past contact with the specific antigen. On the other hand, infection rarely occurs without agglutinins appearing some time at least during the course of the disease.

RELAPSING FEVER

During the past five years, 60 cases of relapsing fever have been reported in California. This is a summer disease contracted for the most part by vacationists in the Sierra Nevada ranges, known cases having been reported from Big Bear Lake in San Bernardino County and from Lake Tahoe south to Sequoia National Park in the central Sierra Range. There is reason to believe that many additional cases occurred which were not diagnosed or not reported. The laboratory methods that establish the diagnosis are the finding of spirochetes of relapsing fever in stained blood smears of the patient or in blood of mice following inoculation with the patient's blood. This service is available in the state laboratory and the larger local public health laboratories and is provided by some of the larger hospital and clinical laboratories.

RICKETTSIAL DISEASES

In California there occur at least three diseases caused by rickettsiae that present diagnostic problems. These are Rocky Mountain spotted fever, which occurs occasionally in the northern Sierra Nevada Mountain range area; endemic typhus, which appears to be limited to the southern California area south of the Tehachapi Mountains; and "Q" fever, which has been identified within the past year and the total distribution of which is unknown. During the past year it has been most prevalent in the Los Angeles area. In all three of these diseases

the definitive diagnosis rests upon either recovery of the rickettsia from the blood taken in the early stages of the disease or a demonstration of rise in complement fixing antibodies as the disease progresses. The latter specific procedure is now largely replacing the long-used, less specific Weil-Felix reaction which rests on a rise in agglutinin titer to certain strains of proteus organisms. Also it should be noted that *Coxiella burneti*, the causative agent of "Q" fever, does not produce agglutinins to "X" strains of proteus. The recovery and identification of the specific rickettsial agent is a time-consuming and costly procedure not without danger of infection to the laboratory worker. However, the complement fixation tests can be readily carried out. Blood should be collected as near the onset of the disease as possible and again a week to ten days later so that the two tests may be run in parallel in the laboratory. A rise in specific antibody is encountered only in the presence of the specific disease. The presence of complement fixing antibodies in a single blood specimen may mean present or previous infection. At present, as far as the author knows, these diagnostic services are available in California only in the state laboratory.

VIRAL DISEASES

There are a number of diseases caused by viruses in which the laboratory can now aid the physician in arriving at a specific diagnosis. Just as in diseases due to bacteria, the laboratory may recover and identify the specific virus or it may demonstrate rise in specific antibodies to the virus in the serum of the patient. The latter, as in rickettsial diseases, is the more simple and practical procedure. The rise in specific antibodies is demonstrated in various ways. One is by the complement fixation test using a specific viral agent as antigen; a second is by the demonstration of virus neutralizing antibodies by observing the effects of properly balanced virus serum mixtures in laboratory animals.

Some indirect procedures have also been developed such as the chicken cell agglutination inhibition reaction in influenza and the occurrence of cold agglutinins in virus pneumonia. Currently such routine diagnostic services in California are offered in the state laboratory. Certain of the tests are also available in a few hospital and clinical laboratories. Such services include tests for influenza, types A and B; virus pneumonia; psittacosis; the various encephalitides due to either Western equine or St. Louis viruses, and encephalitis due to the mumps virus. In addition, complement fixation tests are available for lymphogranuloma venereum and lymphocytic choriomeningitis. In all of these tests the physician should send in both an acute and convalescent blood specimen, the first taken at the earliest possible moment in the course of the infection and the second, ten days to two weeks later.

During the past several years, the State Viral and Rickettsial Disease Laboratory has been studying and developing diagnostic test procedures. As the program during this formative period was largely investigative there were frequently long delays in getting reports back to physicians. Now that a number of the procedures have become routine tests involving complement fixation, results can be reported within a day or two after the second specimen is received. The laboratory diagnostic service available for a number of the viral and rickettsial diseases is therefore now comparable to the agglutination test service available for the diagnosis of typhoid fever. As the various procedures in the viral and rickettsial field are perfected and simplified diagnostic tests are achieved, the services in this field will undoubtedly come to physicians in their own communities through well equipped hospital, clinical and public health laboratories. This will be the case with the more common viral and rickettsial infections; but with rarer infections such as Rocky Mountain spotted fever, psittacosis and the various encephalitides it will probably not be economical for more than one or a limited number of the laboratories in the state to provide such services to the physicians.

SUMMARY AND CONCLUSIONS

It will be seen from the above discussion that the cardinal principles for the clinicians to keep in mind in the diagnosis of communicable or infectious diseases are that an attempt should be made either to recover and identify the specific organism or to provide the laboratory with an acute and convalescent blood specimen so that rise in titer of specific antibodies may be demonstrated. Either of these two fundamental procedures will provide the physician with a definitive diagnosis by the laboratory. As indicated, since a number of these diseases occur so infrequently and the laboratory techniques are new and not readily available, particularly for the viral and rickettsial diseases, the physician must depend for the time being upon the state laboratory for such service. However, as pointed out with the various diseases, in a number of instances services are available through the usual clinical and hospital laboratory channels upon which the physician depends. The logical procedure for the physician to follow is to secure all available services from the laboratory ordinarily serving him, call upon the local public health laboratory for services not provided by his clinical and hospital laboratory, and refer only those specimens to the state laboratory for which no local services are available. At present, the latter are almost entirely limited to viral and rickettsial disease specimens. As this field of laboratory diagnostic tests develops, undoubtedly more and more laboratories will be able to offer diagnostic service in this field.

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The Late Results of Uretero-Intestinal Implantation

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THERE are three procedures for the permanent diversion of the urine from the bladder—implantation of the ureters to the skin, implantation into the intestinal tract, and nephrostomy. The objections to the first and third are obvious. Very few surgeons now use either when intestinal implantation is feasible. Exstrophy and infiltrating carcinoma of the bladder are the two common abnormalities which require permanent bilateral diversion of the urine. Ureteroenterostomy is now standard treatment for the former and is being used more and more in connection with cystectomy for cancer. There is reason, therefore, to review the late results of uretero-intestinal implantation.

The author's records show that 135 patients, 31 with exstrophy, 84 with vesical carcinoma and 20 with intractable conditions (nine with incurable vesicovaginal fistula, 11 with tuberculous cystitis and with hopelessly contracted bladder) have had ureteroenterostomy. Exstrophy can be successfully repaired after diversion of the urine without after-effects and therefore gives the best opportunity of knowing the long term survival, the state of health and rehabilitation, after ureteral transplantation in itself.

The late results after transplantation in the other conditions, cancer particularly, are affected by the degree of success in the treatment of the malignant lesion. These facts are of vital importance in the cure of the conditions, of course, but complicate the picture so far as survival from the transplantation itself is concerned. The late results in exstrophy, therefore, give a truer picture of what to expect from the implantation of the ureters into the bowel as a surgical procedure alone. There is, however, this difference: Ureterorectosigmoidostomy usually is done in infancy or early life for exstrophy, but always in late adulthood or even senescence for cancer, and the older patients frequently already have back-pressure changes in the ureters and kidneys which also affect the result. This back-pressure change occurs sometimes in exstrophy when its correction is too long delayed. If there were no recurrence of cancer after transplantation and back-pressure changes were not present in the upper tract before, the late results in the two conditions with normal upper tracts should be about the same except for the difference in expectancy of life. As every child born in this country now has a life-expectancy of over 65 years, operation in infancy permits the observation of a life-span and will tell how long and in what state of health an individual can live after the ureters have been implanted permanently to drain all the urine into such a highly and continuously infected field as the rectosigmoid—requiring adjustment to a state comparable to that which is natural in aves and in some reptilia (ureters opening into the cloaca).

Twenty-five of the 31 patients with exstrophy are living. Four were surgical deaths. Two patients died of acute peritonitis five and eight days after transplantation by the Coffey method before the days of succinylsulfathiazole (1925 and 1930). A modification of the submucous principle,* a principle so well popularized by Coffey in 1912, has been used since 1934 without one instance of peritonitis. This modification consists essentially in anchoring adventitia of the ureter to submucosa of the bowel at the point of its penetration by the ureter. In those patients in whom the wall of either ureter is thin from dilatation, these anchoring sutures cannot be used with safety on account of the risk of puncturing it, with subsequent leakage of urine. The Coffey-Mayo technique has been used as a rule in those instances. With the advent of succinylsulfathiazole, however, the risk of peritonitis is minimal provided whatever method is used is secure against leakage afterwards.

A third patient, four months old, with exstrophy died 2 days after operation and at autopsy, extensive necrosis of the ends of both ureters with leakage was found. The reason for such early operation, namely a relatively sterile bowel, is no longer valid with succinylsulfathiazole and the embryonic condition of the tissues as found in this patient increases the surgical risk. Between one and two years is now thought to be the optimum age for operation. The fourth case, a child of 16 months, died from an anesthetic. With improved methods of preparation and technique (removing the risk of peritonitis), the surgical risk may be estimated conservatively for this group to be well under 5 per cent. The other deaths occurred, respectively, seven years and nine months after operation. The cause of death of the former is unknown. On last examination, five years after operation, he was well, but his mother wrote in answer to a questionnaire after his death: "He had sick spells at intervals when he lost appetite and much weight but had always rallied quickly and built up strength. He was able to attend public school and had just been promoted to the third grade. He was not quite as active as other children, but was well and quite a happy little fellow most of the time." It is probable, therefore, that death followed an attack of recurrent pyelonephritis.

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*"The Technic and Late Results of Uretero-intestinal Implantation, and Cystectomy for Cancer of the Bladder." (The original report was published in September, 1939, in the Transactions for the Seventh Congress of the International Society of Urology scheduled to be held in New York but postponed on account of the war. A revision was presented August 26, 1947, in St. Moritz, Switzerland at the Seventh International Congress, and will be published in the 1947 Transactions.)

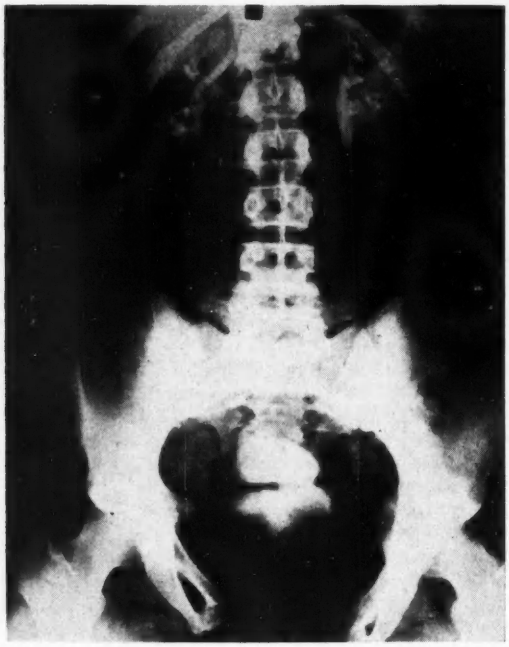

Figure 1.—Photograph of an intravenous urogram taken July 28, 1947. The left ureter was implanted into the rectosigmoid in 1919, the right in 1920 and a plastic repair of the external genitalia was done in 1924. She has been and still is well and active. She married, became pregnant, had an uncomplicated period of gestation and was delivered of a normal child by Cesarean. Urinary control is perfect and nocturia rarely occurs. So far as one can judge clinically, she has never had an attack of pyelonephritis. One could imagine no more perfect result.

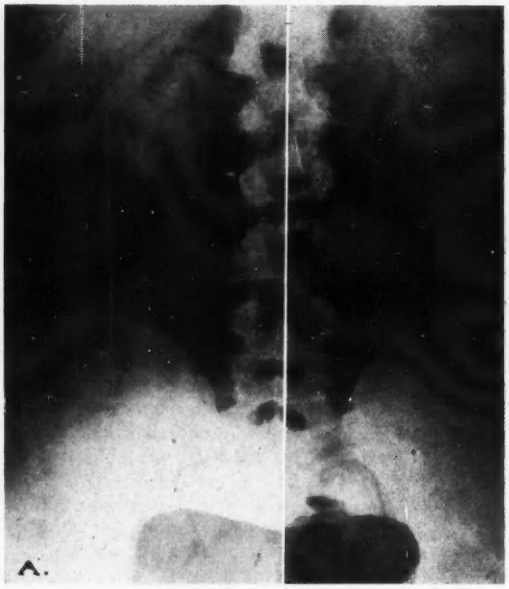

Figure 2.—Photograph of an intravenous urogram (a, right; b, left) taken in June, 1946, 14 years after bilateral ureterorectosigmoidostomy at the age of 10 years, showing some hydronephrosis on the right.

The cause of death in the latter case was some form of shock following cystectomy and plastic repair of the external genitalia. The note on her history is as follows: "Patient was returned to the ward in apparent good condition. However, within a very few minutes she became cyanotic, respirations ceased, and she expired. Efforts at resuscitation failed. Permission for autopsy was granted. No cause could be found at autopsy for the child's death. Moderate bilateral hydronephrosis, moderate hydro-ureters. The openings into the bowel were patent, well healed with little inflammatory reaction. There was no gross evidence of pyelonephritis."

Of the 25 patients with exstrophy who are living, 18 have survived more than six years, seven of these more than 10 years and four of these more than 15 years since operation. Of these four, three are in good health 28 years (Figure 1), 18 years, and 15 years (Figure 2) respectively, two with normal-looking ureteropyelograms; the fourth was as well as the others for 20 years and had married but for some unknown reason then began to have attacks of pyelonephritis with pyelographic evidence of urinary back-pressure (the regular follow-up series of intravenous urograms before having been normal). Unilateral nephrectomy and permanent nephrostomy on the other were performed since which the patient has been getting along quite well for the last two years (it is 23 years since the original ureteral transplantation). Another patient surviving 12 years had to have permanent nephrostomy 10 years after operation, and still another 10 years after ureteral transplantation shows well-marked hydronephrosis which may require nephrostomy later. This patient had considerable hydronephrosis when operated on. Some of the remaining 19 patients have occasional attacks of fever, readily controlled by the modern urinary antiseptics, and most of these show varying degrees of ureteropyelectasis, present however in many of them before operation; a majority of the 19 are in good health.

This review of 31 patients with exstrophy of the bladder indicates that a long term survival in good health can be expected after successful ureteral transplantation into the rectosigmoid and the risk of the method therefore does not contraindicate its use in the radical treatment of cancer of the bladder.

Hemagglutination by Viruses—Its Biological Implications

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THE host-parasite relationship in most virus infections is understood poorly because the physical and chemical processes governing the initial virus-host cell interaction have not been accessible to analysis. An understanding of these processes seems of the greatest importance if any advance is to be made in the systematic and not haphazard study of drugs with possible chemotherapeutic action in virus diseases.

The recent literature indicates that progress of great potential significance has been made, permitting a better understanding of the mechanics of some infectious diseases. Research workers investigating the dynamics of hemagglutination by viruses have reported findings which permit a glimpse into the mysteries of virus-host cell relationships. This review presents briefly some of the more important steps in the investigations which led from the discovery of an apparently simple phenomenon, hemagglutination, to the experimental proof that certain chemical substances may interfere with virus multiplication through the blocking of virus enzymes.

The simultaneous discovery by Hirst[14] and McClelland and Hare[21] of the phenomenon of red cell agglutination by influenza viruses was in itself a development of great significance. It provided an exceedingly simple and efficient method of determining the virus content of materials in the test tube, whereas all previous methods were tedious and expensive, using large numbers of experimental animals for virus titrations.

In the hemagglutination test, serial dilutions of virus-containing material are mixed with red blood cells from human, chicken, or guinea pig and the pattern of the settling red cells is observed in 45 to 90 minutes. In the presence of influenza viruses the cells clump in a characteristic fashion. This reaction is specifically neutralized by the serum of immune animals and man. The hemagglutination-inhibition test has formed the basis for the extensive studies on the epidemiology of influenza and the efficacy of vaccines to produce specific antibodies. The methods for this test have been well standardized[23,29] and provide a useful diagnostic tool for the clinical laboratory.

It was believed at first that only viruses of the influenza group possessed this hemagglutinating capacity. Soon it was demonstrated, however,[1,20] that the agents causing two diseases of chickens, Newcastle disease and fowl plague, also agglutinated red cells; and in 1945 mumps virus, grown for the first time conveniently in embryonated hen's eggs,[13] was added to the list.[18]

The mechanism of red cell agglutination appeared similar to that of the clumping of bacteria by specific antisera: The bridges between red cells were virus particles instead of antibody molecules, and the clumps of erythrocytes settling to the bottom of the tube carried with them most of the active virus. A significant difference from ordinary antigen-antibody reactions became evident when it was demonstrated[15] that red cells could be freed from the absorbed virus by incubating them at 37° C., and if resuspended, these same cells could not be agglutinated again by adding fresh virus. The virus eluted at 37° C. from the cells had lost nothing of its infective power or its hemagglutinating ability for other erythrocytes. In fact this virus material could be used over and over again to hemagglutinate and "stabilize" considerable quantities of red cells, suggesting that its activity was that of an enzymatic destruction of the receptor on the cell to which it attached. Subsequently[16] it was shown that similar processes occurred between influenza virus and its receptor cells in ferret lungs. Hirst[16] concluded from this work that the first step in virus-host cell interaction—that is, infection—was an adsorption of the virus to the susceptible cell and subsequent enzymatic destruction of a specific component of the cell surface to which the virus had attached. The nature of this important surface constituent remained unknown for the time being.

Unexpected relationships among hemagglutinating viruses became apparent when Burnet formulated the concept of the "receptor gradient."[21] The observation had been made that red cells treated with one virus and resuspended became inagglutinable by the same virus but retained agglutinability by other agents. This suggested the possibility that each virus might have a more or less specific point of attachment to the cell surface. Once this "receptor" had been destroyed by the action of one virus, only heterologous agents could attach to the cell's remaining receptors. Hemagglutinating viruses could be arranged in a series, indicating their relative affinity for surface receptors: mumps, Newcastle disease, influenza A, influenza B, fowl plague, swine influenza. Red cells resuspended after agglutination by any virus in this "gradient" could still be clumped by any virus following, but had become inagglutinable by viruses preceding it in the series. After agglutination with swine influenza virus, the resuspended cells often clumped spontaneously or when mixed with normal sera. This non-specific red cell agglutination resembled the phenomenon observed by Thomson[27] and Friedenreich[8] in blood specimens

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accidentally contaminated with bacteria, especially diphtheroids and vibrios. Substances produced by such bacteria could be adsorbed to, and eluted from, red blood cells, just as with influenza virus, and they similarly changed the character of erythrocytes. Such enzyme-like materials of high potency were obtained from anaerobic bacilli[22] and cholera vibrios,[4] but many other organisms produce red cell agglutination[12] and may form similar products.

The Australian workers[24,3] studied filtrates of cholera vibrio cultures in great detail. It was found that these preparations made erythrocytes inagglutinable by influenza viruses, that they were inactivated by heating, and could be neutralized by specific antisera. They were designated "receptor destroying enzyme"[3] because their enzyme-like action resulted in removal of surface receptors for virus particles and in a change of the surface pattern of red cells: Treated Rh positive cells could be agglutinated by "blocking" as well as by complete antibody, and could be hemolysed by fresh normal guinea pig serum.[24]

In view of the fact that this "receptor destroying enzyme" interfered with the attachment of virus to red cell it was of interest to determine its other effects on virus-host cell relationships. Such studies were performed in animal lung tissue and in the allantoic cavity of chick embryos.[5] It was demonstrated that this enzyme promptly liberated viruses of the influenza group which had been adsorbed to host cells, and that it prevented such adsorption if administered prior to the virus.

Much evidence suggests that this "receptor destroying enzyme" is a mucinase, an enzyme that attacks protein-polysaccharide complexes such as mucin. Several mucins are known to be present on the surface of red cells; and the substance carrying O, A, or B blood group specificity, for example, is a mucin. It was suggested therefore that blood group substances might actually be receptors for virus attachment. Soon it became clear, however,[9,6] that purified O and A group substances did not inhibit hemagglutination and thus apparently did not enter into reaction with the virus. On the other hand several investigators reported a variety of polysaccharides which interfere with hemagglutination or virus multiplication.[11,26]

It appears justified, therefore, to postulate that for the group of influenza-like viruses at least, a polysaccharide, or mucin, on the cell surface may be the point of attachment for the virus. Since adsorption of the virus to the cell surface is probably a prerequisite for cellular infection, the presence of such a polysaccharide may determine whether a cell is potentially susceptible to infection. Support for the hypothesis that polysaccharides are of great significance in virus-cell relationships is provided by the following facts:

1. Hemagglutination by viruses of the mumps-influenza group is inhibited by many more or less complex carbohydrates, from apple pectin to red blood cell extracts.[11,6]

2. The hemagglutination-inhibition effect of various sera[7] is abolished by the "receptor destroying enzyme" and by agents which specifically attack proteins (trypsin, for example) and carbohydrates (potassium periodate). This suggests that the inhibitor in serum may be a polysaccharide-protein complex.[5]

3. Saline extracts of various human and animal tissues inhibit hemagglutination by viruses of the mumps-influenza group.[9] Purified preparations from human red cells and lung tissue which strongly inhibited hemagglutination, proved to be at least 50 per cent polysaccharide by chemical analysis.[6] Filtrates and autolysates of pneumococci (containing much polysaccharide) inhibited red cell agglutination by influenza A virus.[25]

4. Takahashi[26] reported that the multiplication of tobacco mosaic virus could be inhibited by a polysaccharide obtained from yeast.

Most of this evidence is admittedly of an indirect nature, dealing chiefly with the phenomenon of hemagglutination as indicator of the participation of polysaccharides in the early adsorption of virus to tissue cells. Since such chemical compounds are known to occur on cellular surfaces it seems important, however, not to neglect their potential significance.

In studies of bacteriophage-host cell relationships it has been demonstrated clearly with the aid of the electron microscope[19] that adsorption of the virus particle to the surface is the first step in infection of the cell. Such adsorption is chiefly determined by the pattern of surface structures, responsible for the high specificity of these bacterial viruses. That similar specific surface reactions may be important in hemagglutination by viruses is indicated by the following findings: Influenza virus A (PR8 strain) agglutinates red cells of humans and chickens but not of sheep, while mumps virus clumps all three types. Extracts of human cells inhibit all these hemagglutinations, but extracts of sheep cells inhibit only agglutination of sheep cells by mumps virus and not that of human or chicken cells by influenza virus.[6] Thus it appears that the specific inhibiting substance present in the extract (principally of polysaccharide nature) is present on the surface of the cell and may well be responsible for initial virus adsorption.

A similar specific relationship has been demonstrated in a different virus-host system.[28] The susceptibility of animal species to infection with pneumonia virus of mice is proportional to the concentration of a lung tissue component which specifically combines with the virus. Little is known about the chemical nature of this tissue component, but it is interesting to note that multiplication of this virus in susceptible lung is inhibited by several polysaccharides.[17]

The facts presented suggest the possibility that in other animal and human virus infections similar conditions might prevail. It has been proposed[5] that the cellular tropism of viruses may be partly based on the presence of specific chemical sub-

stances on the surface of potentially susceptible cells. The mere presence of this surface structure would, of course, not make the cell susceptible, as evidenced by the presence of specific polysaccharides on red cells which are not invaded by viruses of the influenza group. Viruses possessing enzyme systems specific for such compounds could attach to such cells, whereas cells devoid of these surface structures would be susceptible to virus action.

If it is postulated that a virus has to attach to a specific chemical compound on the cellular surface prior to invasion of the cell, then a corollary postulation might be the possibility of blocking this adsorption by similar chemicals. Materials related to the original enzyme substrate could be administered to the host in order to compete with tissue cells for virus enzymes. Such blockage would offer an excellent method of chemoprophylaxis and chemotherapy of virus infections. Recent reports indicate that this possibility is not altogether idle speculation. Green and Woolley[11] found that several polysaccharides inhibited influenza A virus multiplication in the allantoic fluid of fertile eggs. Horsfall and McCarthy[17] showed that polysaccharide preparations lessened the severity of infection with pneumonia virus of mice and inhibited virus multiplication. Ginsberg, Goebel and Horsfall[10] were able to demonstrate that the multiplication of mumps virus in chick embryos could be inhibited by a polysaccharide from Friedlander's bacillus. Except for the large viruses of the lymphogranulomapsittacosis group which respond to a number of drugs, this is the first evidence of a useful avenue of approach to the chemotherapy of virus infections. A great volume of work will probably be done in this direction in the immediate future. Even if it should be shown that the effect of polysaccharides is one of competition for virus enzymes not limited to the cellular surface, this would detract little from the value of the stimulation stemming from interest in the mechanism of hemagglutination.

SUMMARY

Some of the more important steps in the investigations on the mechanism of hemagglutination by viruses have been traced. Like pieces of a jig-saw puzzle, apparently unrelated experimental results begin to fit into a pattern which may open the way for better understanding of the dynamics of virus infection of cells and possible approaches to the chemotherapy of virus diseases. The following advances have been most notable:

1. Respiratory viruses of the mumps-influenza group are able to clump red cells by attaching to a specific substance on the cell surface.

2. The point of attachment, or "receptor," is destroyed by enzymatic action of the virus, as well as by enzymes from a number of bacteria and other sources.

3. Enzymes destroying the "receptor" of host cells for this group of viruses, are specific for more or less complex polysaccharides.

4. It is concluded therefore that the virus "receptor" is of polysaccharide nature, on the cell surface. This is supported by the fact that polysaccharides from a variety of sources inhibit adsorption of the viruses to host cells.

5. This primary adsorption is a preliminary step to the infection of the cell. If it can be interfered with, cellular infection can perhaps be prevented.

6. The early interaction of virus and host cell seems to be based on a virus enzyme acting on a specific chemical substrate of the cell. In the group of mumps-influenza viruses this substrate appears to be a polysaccharide.

7. It may be possible to interfere with this enzyme-substrate reaction, thereby preventing early virus action on the cell. This interference may be possible by introducing material similar to the cellular substrate of virus enzymes. Such material, competing for virus enzyme with tissue cells, may provide for effective chemoprophylaxis and chemotherapy.

8. In a few virus infections it has actually been shown that polysaccharides from a variety of sources have definite chemotherapeutic action under experimental conditions.

ADDENDUM

Since this review was submitted for publication much evidence has appeared supporting the affinity of mucoproteins and viruses of the mumps-influenza group. Such mucoproteins were found in egg white and in normal allantoic fluid suggesting a source of error in laboratory tests using hemagglutination techniques. The work on substances blocking the attachment of viruses to host cells has been extended but there has been no further and more definite indication of the chemotherapeutic significance of this mechanism.

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Changes in the Urinary Tract in Pregnancy

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CERTAIN changes occur in the urinary tract in pregnancy which it is important to recognize because they may closely simulate disease. Unless they are clearly recognized for what they are, misinterpretation of their significance may lead to unjustifiably drastic measures and thus much harm to the patient. Beyond the question of proper interpretation, the chief consequence of the changes is an increased tendency to develop urinary tract infection, usually pyeloureteritis.

Autopsy examination and, more recently, pyelographic study have revealed that there is some degree of dilatation of the ureters and kidney pelves in the majority of pregnant women which is most marked between the fourth and eighth months of gestation, but may not disappear completely for four to six weeks postpartum. These changes are more common in the primigravida for reasons that are not entirely clear, but possibly because the tauter anterior abdominal muscles produce a greater pressure of the pregnant uterus against the ureters. The dilatation is usually greater on the right side. The capacity of the kidney pelves may increase from a normal of 5 or 10 cc. to three or four times that amount. In the non-pregnant state such changes would properly be considered pathological. It is this difference which pregnancy is responsible for which is so important to recognize.

A number of structural and functional changes appear to be associated with the ureteral dilatation. Possibly these changes are causative. There is hypertrophy of the muscle cells of the muscular coats, particularly the circular fibers, resulting in considerable thickening of the ureteral walls, most marked in the intraligamentary portions. Since the characteristic dilatation of pregnancy occurs from the pelvic brim upward, and only rarely below this point, and since the dilatation is most pronounced on the right side while the muscle hypertrophy is equally marked on both sides, it does not seem credible that this change can be more than a contributing cause. A functional change of probable prime importance is the loss of tone of the musculature of the ureteral walls. Normally the ureteral walls are constantly engaged in peristaltic activity which is believed to be the mechanism by which urine is moved from the kidney pelvis to the bladder. Traut and McLane have demonstrated that in pregnancy there is a marked diminution in the peristaltic activity, and it is their belief that this is one of the chief factors in the dilatation of the ureters and kidney pelves and backing up of the urine.

The smooth muscle hypertrophy and the atonia of the ureteral walls are most probably responses to the hormonal changes of pregnancy and are similar to the effects which are produced in uterine musculature at this time. It is not strange that similar effects should be produced in these muscular structures, which have such a close embryological relationship. The mullerian duct from which the uterus is derived, and the metanephric duct from which the ureter is descended, first develop in the same mass of mesenchyme on the postero-lateral aspect of the coelomic cavity, and lie almost side by side at that early period in their development when the mesodermal cells become differentiated to become the muscle cells of their muscular coats. The particular hormones which appear to be responsible for these changes are estrin and progesterone, both of which are present in increased amounts during the greater part of pregnancy. Hundley has demonstrated experimentally that estrogens, in addition to their well known property of stimulating hypertrophy of the smooth muscle elements of the mullerian duct system and the closely associated ureters, cause an increase in the peristaltic waves of the ureteral walls. On the other hand progesterone was found to diminish the peristaltic activity of the ureters. These findings fit in with the accepted actions of these hormones upon the uterine musculature and are probably substantially correct.

Mechanical factors probably also play a major role in the production of ureteral dilatation in pregnancy, and indeed they were the first to be incriminated, long before hormones were known to exist. Pressure of the enlarging uterus probably contributes considerably. Dextrorotation of the uterus which is very common may cause some slight angulation of the ureters and thus constitute a factor. In fact dextrorotation plus the difference in the relationship of the ureters to the vessels and the bowel at the brim of the pelvis on the two sides may possibly explain the preponderance of right sided dilatation. Also in favor of pressure of the enlarging uterus being a chief factor in producing dilatation of the upper tract is the absence of such changes in pregnant animals in which the horizontal position of the body removes the possibility of pressure (although the hormonal changes are similar to those found in humans) as well as the absence of dilatation in cases of ectopic pregnancy and hydatid mole in which the characteristic hormonal changes of pregnancy are present without the usual pressure relationships.

The picture which results from these gestational changes is quite distinct—in fact, so distinct as to

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be startling to the uninitiated. In the non-pregnant state dilatation of the degree seen normally in pregnancy would be definitely pathological. It is very important, therefore, for those who have occasion to deal with such cases to recognize the physiological change and to refrain from unduly drastic measures to alter it. I refer particularly to interruption of the pregnancy, the interdiction of future pregnancy, and the like. It must also be realized that some degree of ureteral dilatation during pregnancy may actually be due to a pathological condition. In the presence of repeated urinary infections, permanent damage to the ureteral walls may have occurred, in the form of fibrosis, so that a return to normal cannot take place. It is important, therefore, to repeat visualization of the urinary tract a month or two after the termination of the pregnancy in all cases in which considerable ureteral dilatation has been demonstrated during pregnancy, or in which infection has been repeated or persistent.

Other changes in the urinary tract in pregnancy, such as those which occur in the bladder, have not been discussed because they are of less importance and are not pertinent to the point of this discussion.

SUMMARY

Some degree of hydroureter and hydronephrosis is physiological in pregnancy and requires no action except recognition if infection is not present. Characteristics of the urinary tract changes are reviewed and the importance of recognizing that the changes are not pathologic is emphasized.

General Surgical Complications of Pregnancy

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GENERAL surgical complications occurring during pregnancy may present formidable problems in diagnosis and treatment. In recent years many former risks to the mother and fetus have been reduced as a result of the accumulated experience in handling these relatively rare cases and by the many advances that have been made in medical science.

In this presentation the more common major, general surgical complications of pregnancy (exclusive of those involving the pelvic organs) will be considered briefly.

ACUTE APPENDICITIS

Acute appendicitis is the commonest abdominal emergency occurring in the pregnant woman. Reports as to incidence vary widely and it is not always clear that only the acute cases are included in the various statistical reports. In five of the reported series studied[2,7,8,22,26] the incidence of acute or subacute appendicitis varied from 17 cases occurring among 16,543 deliveries to 20 cases occurring among 66,431 deliveries. Thus, it is quite obvious that pregnancy does not predispose to acute appendicitis unless there is a history of previous attacks. Most authors agree that recurrent attacks are likely to occur during pregnancy, and in two of the series studied[2,16] the incidence of recurrent attacks was given as 50 per cent and 62 per cent, respectively.

Many authors[2,7,16] report the majority of their cases in the first and second trimester, although in two of the series studied[8,22] the majority of cases occurred in the last trimester. Child and Douglas[7] are of the opinion that actually appendicitis is quite as common in the latter months of pregnancy but that the diagnosis is less frequently made. As they point out, this seems quite logical because the large gravid uterus makes the diagnosis more difficult. Furthermore, the abdominal signs and symptoms that often appear late in pregnancy are difficult to evaluate. Although many attacks of acute appendicitis subside spontaneously and may not have been recognized, it is significant that most series show that the majority of cases of ruptured appendix with attendant serious complications occur in the third trimester.

A ruptured appendix is much more serious in the pregnant woman due to altered anatomical relationships and physiological changes. The omentum and loops of intestine which usually assist in the process of localization are crowded out of the way by the growing uterus, the appendix and cecum may be displaced upward after the third month so that pelvic localization is less likely in the ruptured appendix, and the uterus tends to prevent localization due to its changes in position. These factors, together with physiological increased vascularity and lymphatic dilatation, greatly favor a generalized peritonitis with absorption of septic material, abortion or premature labor and possible death to the prospective mother.

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Success in the treatment of acute appendicitis depends on early diagnosis and prompt removal before rupture of the appendix. The earliest symptom is pain, at first epigastric and later shifting to the right lower quadrant, but this pattern may vary as in the non-pregnant patient. Nausea and vomiting may or may not occur. A slight to moderate fever may be present.

Localized tenderness over the region of the appendix, the most consistent sign of appendicitis, must never be regarded lightly. Involuntary muscle spasm may or may not be present. In evaluating the abdominal tenderness it is well to remember that, in some cases at least, the appendix is displaced upward. Baer[2] and his associates, in a roentgenological study of 70 pregnant women with normal appendices, found that in 88 per cent the appendix was located above the iliac crest after the seventh month. Twyman, Mussey and Stalker,[28] however, in reporting on 75 cases of appendicitis during pregnancy state that at operation, "marked displacement of the appendix was not evident in most cases." It must be remembered that pregnancy is accompanied by a physiological leukocytosis and that a normal white count may be as high as 12,000 to 15,000. An increase in the polymorphonuclear cells, however, is significant. A very helpful diagnostic point is the history of previous attacks and, since this is a particularly significant point in pregnancy, the patient should be carefully questioned in this regard.

A larger percentage of erroneous diagnoses of acute appendicitis in the pregnant woman is to be expected because of the gravid uterus and the multitude of abdominal signs that occur, particularly late in pregnancy. However, because of the seriousness of a ruptured appendix in the pregnant woman, the surgeon must always be on the alert and never procrastinate where he cannot reasonably rule out the condition after a careful differential consideration. Occasionally a normal appendix will be removed or another pathological condition found if this policy of earlier and more frequent operation is carried out, but, as demonstrated by Child and Douglas[7] in their series, "mothers do not die nor are babies lost as a result of an uncomplicated celiotomy."

Careful management of anesthesia is required in the surgical treatment of any complication of pregnancy, and of especial importance is the administration of an adequate amount of oxygen at all times whether the anesthesia is spinal or general.

If one is reasonably sure of the diagnosis of acute appendicitis, a McBurney incision placed over the point of maximum tenderness seems wise even in those cases in which the patient is near or at term. By using this incision one is less likely to disturb the uterus and intestines and the danger of postoperative intra-abdominal and wound complications is less. With the aid of the sulfonamides and penicillin, intra-abdominal drainage is not resorted to as frequently as in the past, but is indicated in the rare case of an old abscess with a thickened necrotic wall, or in a case of general peritonitis where the appendix is not readily located and therefore not removed. Soft drains should be used and they must be placed so as not to come in contact with the uterus or be disturbed by the changes in the position of the uterus.

It is generally agreed that in cases of acute appendicitis the obstetrical factor is to be entirely disregarded except, as Cosgrove[8] has said, the "recognition of the very rare possibility of concurrent serious factors of obstetric dystocia. When this occurs, recourse may be necessary to delivery by the abdominal route. But such interference should be reserved until after the onset of spontaneous labor, and an extraperitoneal approach selected."

Postoperative care differs very little from that given non-pregnant patients, except that sedation and progesterone are used to forestall abortion or premature labor, and enemas and cathartics are avoided for at least four or five days after operation.

GALLBLADDER DISEASE

Since cholelithiasis occurs at least three times more frequently in the female than in the male and 80 to 90 per cent of cases occur in women who have been pregnant at least once, pregnancy has been considered a major factor in the development of this condition.

Biliary stasis and increased blood and biliary cholesterol would appear to set the stage for the development of cholelithiasis in women who have been pregnant. By cholecystographic studies, Gerdes and Boyden[11] have clearly shown that in the second and third trimesters of pregnancy the emptying of the gallbladder is retarded. They attribute this to a "hypertonic condition of the sphincter choledochus, i.e., to a physiological dyskinesia reflecting the changed hormonal content of the organism in pregnancy."

Potter,[24] by direct examination of the gallbladder in a large number of patients delivered by cesarean section at term, found that 75 per cent of normal gallbladders were distended. An analysis of the contents of 58 of these distended gallbladders, withdrawn by means of a sterile needle and syringe at the time of operation, revealed a high cholesterol level and a relatively low bile salt concentration, which is similar to the chemical findings in a damaged gallbladder. As noted, these findings were all in connection with supposedly normal gallbladders and it would appear from these changes and the stasis that there may be damage to the gallbladder wall with alteration of the concentrating power of the mucosa and eventual precipitation of cholesterol. It is worthy of note that Potter[24] rarely found bacterial invasion of the gallbladder bile at term.

Medical management of cholecystic disease can usually be carried out successfully during the course of pregnancy. However, if the patient is subject to repeated attacks of severe gallstone colic, surgical operation is indicated in a quiescent interval if possible. The danger of empyema with possible result-

ant perforation must always be considered and operation done immediately if this condition is suspected.

In the uncomplicated case of cholecystic disease without peritonitis the risk of operation is no greater in the pregnant woman than in the non-pregnant, and cholecystectomy is generally the procedure of choice. However, cholecystostomy is indicated if the patient presents an added risk because of peritonitis or systemic disease, or if there are unusual technical difficulties in removal of the gallbladder. In upper abdominal operations the risk of abortion or premature labor is very small unless peritonitis has developed.

INTESTINAL OBSTRUCTION

Intestinal obstruction occurring during pregnancy is an infrequent but always serious complication. It is most often due to adhesions from a previous operation or adhesions resulting from a previous intra-abdominal inflammatory process. The changing size of the uterus naturally changes the normal relationships of the abdominal viscera, so that adhesions that previously were of no significance may cause kinking and obstruction. Statistics show that the obstruction may occur at any time but is most frequent from the fourth to sixth month of gestation, late in pregnancy and at the time of labor, or in the early days of puerperium.

Some of the less frequent causes of intestinal obstruction in the pregnant woman may be:

1. Congenital adhesions or, very rarely, a congenital defect in the mesentery or broad ligament.

2. Volvulus, which usually occurs in the presence of an abnormally long mesentery and/or improper rotation of the intestines. In 79 cases that have appeared in the medical literature, as reported by Kohn and his co-workers[14] in 1944, the obstructions were localized as follows: "small intestine, 19 cases; large intestine, other than sigmoid, 19 cases; sigmoid, 41 cases."

3. Carcinoma of the large intestine: In 1947 Swartley and his co-workers[27] reported a total of 71 such cases in the literature, including one of their own.

4. Intussusception: In 1937 Chaffin and co-workers[5] collected reports of 19 cases from the literature and added one case of their own in which obstruction was caused by adenoma of the jejunum. In only one other case among the 19 is tumor within the bowel noted, but, as the authors state, "probably such neoplasms were overlooked in some of the cases with undetermined etiology." Enteric ulceration from tuberculosis was a prominent cause.

5. Hernia: This is much less common as a cause of intestinal obstruction than one would suppose. The enlarging uterus pushes the intestines away from the inguinal and femoral canals and most of the reported cases have been due to umbilical and incisional hernias.

6. "Pregnancy ileus": This is merely an intestinal occlusion caused by the growing uterus pressing the sigmoid colon against the brim of the pelvis. The existence of obstruction of this type is probably questioned by many obstetricians and surgeons but it appears to have been firmly established as a rare clinical entity. Ludwig (1913)[15] collected reports of ten cases, Mikulicz-Radecki (1926)[19] collected ten cases, and Eliason and Erb (1937)[10] collected 25 cases from the literature during the period from 1925 to 1935 and added three of their own. Practically all pregnant women are constipated and, as has been pointed out, if there were an added disturbance of the vegetative nervous system "pregnancy ileus" might occur in the later months of pregnancy.

The diagnosis of intestinal obstruction in the pregnant woman is most difficult because many of the cardinal symptoms of obstruction may be seen in normal pregnancy. If the condition is suspected, every facility possible must be used to reach an early decision if one is to avoid the danger of peritonitis with its attendant high maternal and fetal mortality rate. An evaluation of the past history regarding previous operations or previous abdominal or pelvic complaints is important along with a careful appraisal of the present history, physical findings and laboratory studies. An x-ray film of the abdomen to determine the gas pattern is always indicated, although the evidence may not be conclusive. If no gas is found in the small bowel and the symptoms suggest obstruction in the large bowel, sigmoidoscopic examination and/or a barium enema is indicated, depending on the suspected site of obstruction. If the barium enema meets obstruction in the pelvis a tumor is the most likely cause, although the rare possibility of "pregnancy ileus" as a cause of the obstruction arises and, as a diagnostic measure, an enema given in the knee-chest posture is indicated. In two of the three cases of "pregnancy ileus" reported by Eliason and Erb[10] the obstruction was relieved in this manner.

Generally speaking, spinal anesthesia is the best in connection with operations to relieve bowel obstruction as better relaxation is obtained, and thus there is less trauma involved in handling the bowel. In the presence of bowel obstruction one of the greatest anesthetic hazards is the danger of aspiration of regurgitated material. McCuskey[17] states that this can be minimized by using spinal anesthesia preceded by light medication so that the patient is able to cough and keep the trachea clear; or, if a general anesthetic is given, an endotracheal catheter may be used with a balloon attached to completely seal off the trachea.

The surgical results vary directly with the promptness of operation. Simple freeing of adhesions requires little manipulation so there is small danger of peritonitis in the early case and the pregnancy is endangered very little. However, when operation has been delayed, permitting vascular changes that make resection necessary, the dangers mount rapidly. In Eliason's and Erb's[10] collected series of 66 cases of intestinal obstruction covering the period

1925-1935 the maternal mortality rate was 21 per cent and the fetal death rate 50 per cent.

In a consideration of carcinoma of the large intestine Swartley and his co-workers[27] expressed the opinion that there is not enough evidence to support the idea that pregnancy affects an extragenital malignancy to the extent that termination of the pregnancy is indicated. It is quite generally agreed that in early pregnancy the management of the carcinoma should be the same as in the non-pregnant patient. As to carcinoma in the later months of pregnancy, Bonner and his co-workers[3] and Swartley[27] recommend exploratory laparotomy to determine operability. If the carcinoma proves inoperable and there is no obstruction to the birth canal, colostomy is done to permit normal delivery. If operation is feasible and manipulation of the female organs is necessary, cesarean section, hysterectomy, and resection of the lesion are carried out in one or two stages. This eliminates the possibility of miscarriage with the increased risk of peritonitis. When the lesion is outside the pelvis and manipulation of the female organs is not necessary, an exteriorization procedure or an end-to-end anastomosis may be carried out, permitting normal delivery. These radical procedures are carried out, of course, only in cases in which it may be assumed that the obstruction is only partial. Before operation the bowel must have been decompressed by the use of enemas, and there must have been adequate preoperative preparation with sulfasuxidine or sulfathaladine. If the obstruction is complete, as occurs in a very small percentage of large bowel malignancies, colostomy is the only safe procedure and it is to be carried out as a preliminary or final procedure. As in other surgical emergencies of pregnancy, progesterone and sedations are indicated postoperatively.

HYPERTHYROIDISM

A physiological enlargement of the thyroid gland occurs in many pregnant women, as the state of pregnancy demands an increased secretion from this gland. Various observers are essentially in agreement that the basal metabolic rate remains normal during the early months of pregnancy and then, gradually rising in the last three or four months, reaches 20 to 25 per cent above normal at term. This increased rate indicates the response of the thyroid gland to the increasing mass of active protoplasmic or fetal tissue and, to a lesser extent, to an increase in the maternal structures incident to pregnancy.

Although it is not uncommon for pregnant patients to present evidence of nervous instability, careful evaluation of the subjective and objective findings usually will not substantiate a diagnosis of hyperthyroidism which is a relatively infrequent complication of pregnancy. Various statistical reports as to incidence of this disease during pregnancy show a variation from .07 per cent to 3.7 per cent, and in general it is more frequently seen where goiter is endemic.

Of the two distinct diseases of the thyroid gland associated with hyperthyroidism, exophthalmic goiter is found more frequently as a complication of pregnancy than adenomatous goiter with hyperthyroidism.

The normal course of exophthalmic goiter is subject to exacerbations and remissions. Frequently it can be managed through pregnancy with the judicious use of compound solution of iodine (Lugol's solution), sedation and rest. An index which can usually be followed cautiously is that if a mild case of exophthalmic goiter responds with a remission after two weeks of treatment, the patient can usually be carried through the pregnancy in a conservative manner. If the response is not practically or entirely complete, subtotal thyroidectomy is usually indicated except in selected cases in the last trimester of pregnancy.

Adenomatous goiter with hyperthyroidism usually has the tendency to become progressively worse and does not often show a good response to iodine. As is emphasized by Mussey[20] and others, it is usually advisable for the patient to have the adenoma removed. As Mussey[21] states: "Even in the last six weeks of pregnancy, in the presence of a metabolic rate of more than 50 per cent [above normal] which has been maintained for a considerable period, in the presence of myocardial insufficiency or of dyspnea caused by pressure of the adenoma on the trachea, removal of the adenomas prior to delivery of the baby usually is the safest procedure." Also in a case of multiple large adenomas without hyperthyroidism where substernal pressure on the trachea is present it may be advisable for the patient to have the adenomas removed.

Each case must be individualized and, as McLaughlin and McGoogan[18] state, "there can be little doubt that the pregnant woman with hyperthyroidism can successfully withstand a thyroidectomy, but the question remains the necessity and advisability of the procedure in all cases." In the rare instance in which there has not been an adequate response to compound solution of iodine and in which surgical operation is considered too hazardous, x-ray therapy may be tried.

Therapeutic abortion is practically never indicated for hyperthyroidism, as is emphasized by Mussey,[20] Portis and Roth,[23] Baumgartner[4] and many others. In mild cases abortion needs no consideration. In severe cases the possibility of a thyroid crisis arises; abortion does not cure the hyperthyroidism.

The use of Thiouracil and kindred drugs in hyperthyroidism has been modified considerably since their introduction due to some of the severe toxic reactions that have resulted. In the pregnant woman transfer occurs across the placental barrier and hyperplasia of the fetal thyroid has been demonstrated. Also the drug appears in the mother's milk. As Curtis and Swenson[9] state, "Carefully controlled studies on the experimental animal and in man are not yet available to judge the effects of such long continued therapy accurately on either the mother

or the fetus. Widespread use of the drug during the period of gestation should be avoided until further studies are available unless the emergency is dire."

CARCINOMA OF THE BREAST

The development of carcinoma of the breast during pregnancy is fortunately an infrequent occurrence. If it does occur a fulminating growth is likely, as the breast is being prepared for lactation by an increased hormonal stimulation which results in an increased blood supply and a large increase in the glandular and ductular elements. Harrington,[13] in a study of 92 cases in which the tumor was present in the course of pregnancy or lactation, found that in 81.5 per cent the tumors were of either grade III or IV malignancy and that in 84.8 per cent of the cases there was axillary involvement at operation. In this series the five-year survival rate for patients with axillary involvement was 5.7 per cent. However, in those few cases in which there was no axillary involvement the five-year survival rate was 61.5 per cent, which indicates that the condition is not hopeless if recognition is early. Thus, from these grim figures, it is obvious that the obstetrician must be on the alert and make frequent routine examinations of the breast during pregnancy.

If any suspicious discrete mass is found in the breast, removal of the mass and microscopic examination are obligatory; and if it is found to be malignant, radical mastectomy is indicated. Also, because of the usual high degree of malignancy in these cases, x-ray therapy seems indicated regardless of whether the axillary glands are involved or not. Some observers consider all cases which occur during pregnancy or lactation to be inoperable due to the high degree of malignancy.[12]

The question of whether the pregnancy should be ignored in the presence of carcinoma of the breast is important. If the pregnancy is not interrupted most patients will go to term and deliver a normal child even after submitting to a radical mastectomy and x-ray therapy. In the past most obstetricians and surgeons have individualized their treatment of cases but generally have been of the opinion that the pregnancy should be ignored in the presence of carcinoma of the breast. It would appear from Smith's[25] statistical study of a small group of pregnant women with carcinoma of the breast that the prognosis is better if the pregnancy is not interrupted. Recently, however, Chase[6] has advocated interruption of the pregnancy followed by testosterone, radical mastectomy and x-ray therapy. Testosterone has demonstrated its palliative value in many cases of bony metastasis from carcinoma of the breast but only occasionally has a favorable palliative response been noted in the case of a primary tumor or metastases from it to soft tissue. As Adair[1] has pointed out, the field of androgen therapy in carcinoma of the breast is new and a great deal more clinical research must be carried out before a final evaluation of it is made.

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Chemotherapy for Renal Infections

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CHEMOTHERAPY for renal infection has advanced tremendously during the past decade. This has stimulated the growth of a voluminous literature. Out of this plethora of data there is emerging some definitive information which will aid in the treatment of pyelonephritis. If we speak in the main of the better established clinical aspects of renal infection, we do so with full knowledge of the many gaps in our understanding of the basic principles underlying the mode of onset, the pathways of entry and the actions of the bacteria which cause pyelonephritis. Moreover, our understanding of the mechanism of chemotherapy is still fragmentary.

The use of the newer chemotherapeutic agents has greatly increased the effectiveness of treatment but it has not simplified the process. Proper use of these drugs requires intelligent knowledge of various factors which, even today, are too often neglected.

The choice of chemotherapeutic agents in the treatment of renal infections is determined by the type of bacteria found in the urine. While the kidney may be the victim of practically any of the pathogenic organisms, five main groups will encompass the bulk of urinary infections. These, in order of their prevalence are: (1) The E. Coli group, (2) the staphylococcus, (3) the streptococcus, (4) the proteus and (5) the tubercle bacillus. Mixed infections frequently occur. Moreover, cases of typical pyelonephritis have been described in which no causative organism may be demonstrated.[8]

The first principle in obtaining an accurate understanding of the bacteriology of infected urine is proper collection of the specimen. Neglect of this is one of the most common causes of error. The specimen must be fresh and collected in clean containers. In the female patient, a specimen taken by catheter is essential. In the male patient, a carefully collected second glass specimen is usually sufficient. For a complete study, urine catheterized from both kidneys is necessary.

The initial step in the study of the urine is the examination of the fresh urinary sediment; this is followed by staining. The simple stains will give much information. The Gram stain affords more differentiation. Where tubercle bacilli are suspected, special staining must be carried out. Cultures should be used for confirmation of the microscopic findings and for separation of the bacterial sub-groups. Treatment may be initiated on the basis of the microscopic information. Only in special instances should therapy be held up for the more elaborate cultural differentiations. Criteria of cure, of course, are negative cultures.[14]

Brief mention must be made of the determination of the reaction (pH) of the urine. While there is little of diagnostic value in this test, it is of essential importance in intelligent chemotherapy.

Accurate knowledge of pathological processes coexisting within the urinary tract is paramount.[13] Good renal function with absence of foreign bodies and ulcerative lesions, together with free flow of urine, is essential to successful therapy. Simple tests may be used to determine these factors. Renal function may be accurately determined either by blood nitrogen levels or by the excretion dye tests. Simple and rapid estimations of function may be obtained by specific gravity observations. Foreign bodies may usually be picked up by roentgenographic flat films. As a rule, destructive lesions and evidence of obstruction may be determined by excretory urograms. For exact reviews, where definitive pyelographic outlines and collection of urine for bacteriologic and differential functional studies are required, the retrograde cystoscopic examination is necessary. As a rule, the more persistent the infection, the greater must be the effort in evaluating coexisting disease.

EFFECTIVE CHEMOTHERAPEUTIC DRUGS

The present effective chemotherapeutic drugs are mandelic acid, the sulfonamides, penicillin and streptomycin. Each has its role in modern therapy. Their efficacy is in direct relation to the concentration of the drug in the urine and in the tissues. This, in turn, depends upon the dosage, the renal function and the renal volume.[13]

Mandelic acid is effective against the E. Coli, streptococcus fecalis and occasionally against staphylococcus albus. In order to be effective, the urinary concentration must be 0.5 per cent or greater and the urinary pH must be 5.5 or less. It may be given in liquid or tablet form. It is usual to include ammonium chloride as an adjunct. The fluid intake should be limited to 1,200-1,500 cc. daily, and alkaline foods, especially fruit juices, should be omitted. Mandelic acid is contra-indicated in acute pyelonephritis, in cases of decreased renal function and in the presence of high fever. It is not well tolerated in older patients.[9]

The sulfonamide family was the first of the magic bullets. In urinary infections the sulfonamides are effective against all the commonly occurring Gram negative bacilli, the staphylococcus and occasionally, the streptococcus fecalis. Sulfathiazole and sulfadiazine are more useful than the earlier forms.

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The toxic manifestations due to the sulfonamides are well known. They are less frequent with the newer forms. Crystalluria is increased with sulfathiazole and sulfadiazine. Most alarming are the renal complications which result from the poor solubility of these drugs and their acetyl derivatives. This may result in anuria. Two types have been noted, the mechanical anuria in which occlusion of the renal collecting system may result from precipitation of crystals or concretions, and the chemical anuria which is due to acute toxic and degenerative lesions of the renal tubules.[1]

In the treatment of urinary infections the dosage of the sulfonamides may be kept below the critical level at which most of alarming complications occur. Doses of 2 gm. daily for the first two days, then 1 gm. daily for 14 days will usually result in sterilization of the urine in cases where the bacteria are susceptible and there are no complicating uropathies. The question of adjuvant alkali therapy is still under investigation. The majority of studies indicate that alkaline urine increases the solubility of the drug, thus reducing the incidence of renal complications.[5,11,17] At present, it is our practice to give sodium bicarbonate in equivalent amounts with each dose of sulfonamide. In cases of renal or cardiac insufficiency the use of alkali therapy may present a difficult therapeutic problem. Here one must weigh the possibility of edema from the sodium ion against the consequence of renal damage.[1]

Fluid intake with the sulfonamides should range from 1,500 to 2,000 cc. daily. The urinary output must be measured and the drug stopped if the level falls below a litre daily. While crystalluria does not necessitate withdrawal of the drug, it calls for increased vigilance with respect to the possibility of renal damage. The combination of two or more sulfonamides has made it possible to give relatively large total doses of the drug with little tendency to crystal formation.[21]

Relapse following sulfonamide therapy has been noted. It is not so frequent as found with either penicillin or streptomycin. It has been our experience that sensitization to the drug is not so marked as with the newer antibiotics. As a rule the organisms respond equally well to further sulfonamide therapy.

Penicillin is largely eliminated by the kidneys.[2] The amount depends upon the dosage, the method of administration and the renal function. This takes place apparently by filtration through the glomeruli and excretion by the tubules.[20] The excreted penicillin possesses antibacterial properties.[22] This gives a high level of the drug in the urinary channels. It is certain that the blood supply to the tubules contains a higher level of penicillin than is found in the peripheral circulation. This high level within the renal circulation and the urinary channels results in the effectiveness of penicillin in urinary infections.

The mechanism of action of penicillin has not been proven. Studies indicate that it is the result of an interference with a metabolic function concerned in the early stages of bacterial multiplication.

From a clinical standpoint, penicillin has become the most effective agent against the staphylococcus and the streptococcus. Most strains of these two groups are either highly or moderately susceptible. The bacillary group and the streptococcus fecalis show little or no susceptibility. This has been shown to be due to the production by these organisms of a substance capable of inactivating and inhibiting penicillin. Because of the enzymatic nature of this agent, it is called penicillinase. The E. Coli group are particularly capable of producing penicillinase. It is due to this activity that oral and rectal administration of penicillin is of reduced therapeutic value.[20]

Various routes of administration have been studied. At present the usual practice is to use intermittent intramuscular injections. With aqueous solutions, absorption is fairly rapid and there is still an effective concentration in the blood at the end of three to four hours.[27] Our present practice is to administer 25,000 to 50,000 units at intervals of three hours around the clock. Evidence indicates that a four hourly interval will give comparable clinical results. Where the ambulatory patient is being treated, penicillin may be administered in the wax and oil vehicles.[27] The average dose is 300,000 units in 24 hours. Recently, the combination of penicillin with procaine in an oil base has proven very effective.[12]

ORAL ADMINISTRATION OF PENICILLIN

Oral administration of penicillin has been widely used. Effective serum levels may be secured and maintained. The penicillin is absorbed from the stomach and duodenum. It is best given on an empty stomach and the dosage must be several times larger than with the intramuscular route. The present cost of the oral form is still high. This will undoubtedly be reduced in time. Dosage of 100,000 units every two to three hours is advocated.

In urinary infections we feel that medication should be continued for five to seven days. If sterilization of the urine has not been accomplished in this time, it must be assumed that the bacterial strain is not susceptible or that urinary stasis or reduced renal function has prevented the drug from acting upon the organisms. We recognize the value of susceptibility tests upon the bacteria, and where this is practical it should be done. The use of penicillin is not incompatible with the sulfonamides. The combination of the two drugs will prove very helpful in combating mixed infections. There have been some reports indicating a synergistic action between the two drugs.[30]

The toxicity of penicillin is remarkably low. High dosage has resulted in some urticarial and skin reactions. This is most likely to occur with the administration in the oils and beeswax preparations and is probably a reaction to the vehicle rather than to the penicillin.

The use of various preparations to increase the blood levels of penicillin depends upon blocking tubular excretion. While this may be valuable in other systemic diseases, it seems unnecessary in renal infection where excretion through the tubules is beneficial.

Relapse following penicillin is more common than with the sulfonamides. Resistance of the organism can occur. It is not so pronounced as with streptomycin.

Streptomycin was first described in 1944.[28] It was found to be most effective against the Gram-negative bacilli.[26]

Streptomycin is measured in terms of weight of the pure substance.[19] Following parenteral injection, streptomycin is readily absorbed and reaches the urine within one to three hours. Between 60 and 80 per cent is eliminated by the kidneys.[3,4] The rate of renal excretion is slower than for penicillin, probably because streptomycin is eliminated by glomerular filtration alone and does not seem to be excreted by the tubules.[6,25] Levels of the drug in the urine are much higher than those found in the blood. It is interesting that streptomycin in concentrations higher than 200 micrograms per cc. reduces Benedict's solution. This may be used as a rough index of urinary concentration.

In view of the wide variation in susceptibility of organisms and their various strains to streptomycin, it is advisable to determine the sensitivity of the infecting strain as a guide to treatment.

In renal infections, streptomycin is best administered by intermittent intramuscular injections. The dosage depends upon the sensitivity of the organism to the drug, the nature and extent of the infection and the clinical response of the patient. One to two grams daily, in divided doses every four to six hours, is the present recommendation. Treatment should be kept up for five to seven days. The effect of streptomycin is increased in alkaline urine. Except where urea splitting organisms are present, alkalization should be carried out.[10] Oral administration is of no value in urinary infections. While streptomycin is not destroyed by the gastric juice or intestinal secretions, there is practically no absorption through the intestinal tract.[31]

The development of resistance by bacteria to the action of streptomycin is of great practical importance. The mechanism is not known but its effect has been observed by numerous workers. It is the primary cause of failure in therapy. This proves the importance of giving, from the onset of treatment, adequate doses of the drug in order to control the infection as rapidly as possible before resistance develops. Bacteria which exhibit this tendency to resistance are not likely to lose it in subsequent treatment.[19]

The toxicity of streptomycin is greater than that of penicillin. Where therapy is of relatively short duration, the toxic manifestations which often accompany prolonged administration of large doses are rarely encountered. The milder reactions consist of elevation of temperature, arthralgia and skin rashes. While these may be due to individual sensitivity of the patient, there is much evidence that some of them result from a histamine-like reaction due to impurities in the drug. The newer products have shown less of this type of impurity. As a rule these milder reactions do not necessitate withdrawal.

The more serious complications consist of neurotoxic signs such as vertigo, locomotor disturbances, tinnitus and, more rarely, deafness, apparently the result of a selective toxic action on the eighth cranial nerve. In cases where streptomycin is to be given in high doses for a prolonged period, the patient should be warned of the possible occurrence of such symptoms. If such disturbances continue, the drug should be discontinued.[23]

The value of streptomycin in urinary tract infections has been established. In a survey for the National Research Council, Keefer and his group[24] reported a relatively high recovery rate in cases in which penicillin or the sulfonamides had failed. Uniformly poor results have been reported in patients with neurogenic bladders. This has been attributed to the presence of catheters, suprapubic fistulae, calculi and residual urine.[18] Such cases have always been refractory to treatment; mixed infections are usual.

Streptomycin has been found of value in the treatment of tuberculosis.[29] Some series have been reported on its use in urinary tract involvement.[16] The symptomatic improvement of lower urinary tract lesions is impressive and a few instances of disappearance of tubercle bacilli from the urine have been observed. There was a large percentage of recurrence of the infection. This indicates that the tubercle bacillus rapidly becomes resistant to the drug.[15] Where streptomycin is used in urinary tuberculosis, it will probably be necessary to continue the drug for several months. It is not necessary to use the large toxic doses, as ½ gm. of streptomycin once daily seems sufficient to stop proliferation of sensitive tubercle bacilli.

It is still too early to evaluate these results. The combination of streptomycin with promin, one of the newer sulfonamides, is being used in some centers. This may prove helpful in bilateral involvement. At present, the treatment of unilateral renal tuberculosis is surgical.[7]

CONCLUSIONS

The use of the newer chemotherapeutic agents has greatly increased effectiveness in the treatment of renal infections but it has not simplified the process. Proper use of these drugs places new responsibilities upon the physician. He must know what organism is causing the infection and which drug will combat it. He must have an accurate knowledge of the dynamics of the urinary tract. He must be alert to the signs of toxicity. He must be mindful of the possibility of drug resistance. He must keep his patient under constant supervision

and be prepared to vary the treatment with changes in clinical and bacteriological findings. These added responsibilities will be rewarded with vastly superior clinical results.

The ideal urinary antiseptic is yet to be discovered. The tremendous advance made during the past decade has given fresh impetus to the scientific investigator. Clinical medicine must keep step with this progress.

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The Electrocardiogram in Rheumatic Fever

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IN a consideration of the electrocardiographic changes in rheumatic fever, it must be kept in mind that the changes found are not specific for this disease alone. They are resultant from changes in the structure and endogenous chemistry of the heart, such as could be brought about by a variety of etiological factors, and hence, the individual electrocardiographic changes of rheumatic fever are seen in various diseased states. However, in few disease entities is the heart, and hence the electrocardiogram, so frequently involved as in the disease under discussion.

USUAL ELECTROCARDIOGRAPHIC FINDINGS IN ACUTE RHEUMATIC FEVER

In active rheumatic fever each segment of the electrocardiogram may be altered and the rhythm may also be disturbed.

By far, the most common change is an increase in PR interval. In the observations of different investigators, this change has been noted in varying proportions, from the 93.8 per cent of Rothschild, Sachs and Libman and the 84 per cent of Cohn and Swift, to the 5 per cent in the cases of Filberbaum, Griffith, Solley and Leake.[2,5,19,21] Discrepancies such as these are due to various factors. The electrocardiographic changes in rheumatic fever are often fleeting, and hence, the more frequently tracings are taken, the greater will be the likelihood of detecting abnormalities. Thus in the series of Cohn and Swift, 2,591 tracings were taken on 37 patients; in the series of Filberbaum and his coworkers[5] 9,634 readings were taken on 6,000 patients. Another reason for the variance may lie in the stage of illness of the patients observed. Positive findings are common in the active stage but disappear with the subsidence of the disease process. The patients of Cohn and Swift[2] were in an active stage of the disease. A large proportion of the cases of Filberbaum were in men who were several weeks beyond the zenith of the disease. This latter observation does not mean that changes in the PR interval must necessarily occur during the acute fulminant stage. Frequently, prolongations of this segment are observed after the fever and joint symptoms have subsided.[5,21] However, with the return to normal of all other signs of activity—tachycardia, fever, joint symptoms and blood findings—the PR interval in most cases also returns to normal. In a few cases, however, it may persist for weeks and even many months. In these latter cases, permanent damage of the conducting tissue must be suspected.

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The degree of AV delay as demonstrated by the electrocardiogram may vary from findings within the range of normal, through various stages, up to complete dissociation. Dropped beats of the Wenckebach pattern may take place. Great variations in the PR interval may occur in the tracings of a given individual within a short space of time. As was previously noted, these changes are not entirely dependent on other signs of rheumatic fever. Their occurrence, however, in serial tracings, does indicate rheumatic activity.

Cohn and Swift[2] have demonstrated that, in the normal individual, prolongation of the PR interval can occur, probably as a result of vagal influence. However, these changes do not exceed 0.02 seconds. An increase of 0.04 seconds then would be indicative of a pathologic process or function. Thus, an individual whose normal PR interval measured .14 seconds could develop a measurement of .18 or .19 seconds, which, although within the limits of normal for some persons, would be for him abnormal and suggestive of myocardial disease.

QRST CHANGES

The frequency of changes in the QRST or ventricular portion of the electrocardiogram in rheumatic fever, as is the case with PR interval changes, will also vary with the acuteness of the disease process. Thus, in the Rothschild, Sachs and Libman[21] series, QRST changes were noted in 80 per cent of the cases. In a recent series of acute cases observed in an army hospital by Wendkos and Noll,[25] 11 per cent of the patients exhibited changes which were judged significant, while among the 6,000 patients of the Filberbaum study, 7 per cent had changes in the ventricular portion of the electrocardiogram. In the QRS segment deviations from normal varied from the 53 per cent figure of the Libman[21] study to 7 per cent in the study of Filberbaum and his associates. It is our impression that, in part, the higher proportion of abnormalities in the earlier studies such as those of Cohn and Swift[2] and of Rothschild, Sachs and Libman,[21] is due to the inclusion of grades of widening of this complex and of axis deviations which today, in the light of recent studies on large groups of normal healthy individuals, would not be considered significant.[3,6,23,24] Nevertheless, gross widening of this segment beyond the normal of the individual under observation would be considered important, as would distinct shifting of the electrical axis. Absence of R_{CF4} or R_{V4} is another finding generally indicative of myocardial involvement.

Elevation or depression of the ST portion of the electrocardiogram has been reported to vary from

the 45 per cent figure of Rothschild, Sachs and Libman to the 1.23 per cent of Filberbaum and his associates. The latter authors felt that unless the ST changes were marked or variable, or else associated with other changes in the electrocardiogram, they were in most instances not of great significance. However, when the ST change was marked, or changed from time to time in serial observations, or when it was associated with changes in other segments of the electrocardiogram, especially of the T portion, then this abnormality became definitely important.

T wave changes, namely depression, diphasic character, or inversion, except when occurring as an isolated finding in the third lead, are in general an indication of myocardial or pericardial change. The combination of T wave changes in leads I and II, II and III, I and IV and, as is frequently the case with pericarditis, in all leads, indicates cardiac damage. The association of T changes with ST changes, especially the combination of an elevated ST with a negative T, is apt to be important.

So far as the frequency of occurrence is concerned, we find the same widespread variance in T wave changes as with changes in other segments. Thus, Rothschild, Sachs and Libman[21] report an incidence of 60 per cent, while Filberbaum and his associates[5] report 2.08 per cent involvement. The figures of other observers fall between these extremes. Here the stage of the disease and the frequency of observation play a role.

DISTURBANCES OF RHYTHM

The most important arrhythmia occurring during the course of active rheumatic fever is auricular fibrillation. It occurs with less frequency in active rheumatic fever than in mitral stenosis with rheumatic activity quiescent. When present in acute or subacute rheumatic fever it is usually accompanied by heart failure and it is usually transient in character, ceasing with the subsidence of congestive failure.[29] A group of disturbances interpreted as being indicative of increased sensitivity of the A-V node were found by Filberbaum and his associates[5] in relatively high frequency. Thus, nodal extrasystole, nodal rhythm, nodal tachycardia and ventricular escape were found 25 times in 6,000 patients, an incidence of 0.41 per cent.

Various changes in rhythm or in the electrocardiogram not infrequently occur, but in recent years these have not been thought to be of great significance. Thus, extrasystoles occur scarcely more frequently among patients with rheumatic fever than in normal individuals. Minor variations in the pacemaker would also fall in this category. Changes in amplitude of the P and T segments and shifts of the electrical axis have also been thought less important as indications of rheumatic fever activity.

To recapitulate at this point, the electrocardiographic changes of rheumatic fever are not specific for this disease. The change of greatest frequency is prolongation of the PR interval which may occur in varying degrees up to complete dissociation of auricle and ventricle. After the teaching of Cohn and Swift[2] an increase of over 0.02 seconds in the PR interval should be considered significant. Changes in the PR interval can occur either in the acute or subsiding stage of the disease. Only in rare cases does this change persist with quiescence. Changes in the ventricular portion of the electrocardiogram are also important. Gross changes in the QRS segment are significant as is also an absent R_4. Marked elevation or depression of the ST segment and T wave depressions are significant especially if the two are combined. All these changes are of added significance if it can be shown that they are deviations from the individual's normal tracing. Auricular fibrillation is the most significant of the arrhythmias that can occur during the course of rheumatic fever. Other disturbances of rhythm, those involving the A-V node possibly of greater importance, are not infrequently noted.

A word should here be interpolated that not all patients with rheumatic carditis, even when the disease is severe, show electrocardiographic changes, and also marked electrocardiographic changes can occur without clinical evidence of disease.

THE BASES FOR THE ELECTROCARDIOGRAPHIC CHANGES OF RHEUMATIC FEVER

The widespread involvement of the blood vessels of the heart in rheumatic fever is well recognized. Karsner and Bayless[10] demonstrated involvement of the coronary arteries or their branches in each of 56 autopsies on patients afflicted with rheumatic fever. These authors cite corroborative evidence in the works of many investigators. Myocardial involvement secondary to this vascular change is to be anticipated and has been repeatedly described. Electrocardiographic changes resultant from this pathological change are also to be expected, and are found more frequently in rheumatic fever than in any other common febrile disease. Pericarditis of rheumatic origin also contributes its quota to the altered electrocardiographic patterns. Cardiac enlargement secondary to myocarditis may or may not lead to alteration of the electrical axis. When secondary to valvular defect the resultant chamber enlargement determines the degree of axis shift, if any results.

The origin of the prolongation of the AV conduction time has received considerable attention through the years. Cohn and Swift,[2] in 1924, recorded some slight variation in normal individuals from day to day, and with the phases of respiration. As was previously noted, these changes did not exceed 0.02 seconds. A possible vagal origin was suggested. In 1937, Bruenn[1] reported 22 patients suffering with active rheumatic fever and manifesting prolonged AV conduction time, in 18 of whom the intravenous injection of 1.5 to 3 mg. of atropine sulphate eliminated this defect. In two of these patients, marked emotional stress temporarily re-

duced the conduction delay, thus suggesting a sympathicotonic influence. Epinephrine administration was then found to duplicate these results on both the rheumatic fever patients and the controls. Bruenn concluded that in rheumatic fever the delay in AV conduction was ascribed, at least in part, to increased vagal tone, and he suggested a focus of irritability in the medulla as its source. Shortly thereafter, Keith,[11] in a well controlled study, repeated Bruenn's findings. Keith felt that the origin of the accentuated vagal effect was peripheral and was probably linked up chemically with the inflammatory process in the heart. More recently, Gubner, Szucs and Ungerleider[8] also suggested peripheral involvement as the source of the increased vagal or cholinergic influence, postulating a decreased suppression of cholinesterase, in turn, a result of the increased acidity of inflamed heart muscle. The absence of a general systemic vagotonic effect is offered as additional evidence of peripheral rather than central origin of this finding.

SPECIAL TECHNIQUES IN THE DETECTION OF ELECTROCARDIOGRAPHIC CHANGES IN RHEUMATIC FEVER

Findings such as those noted have stimulated some interesting attempts to utilize this apparent increased vagal tone in this disease to diagnose cardiac involvement. Gubner, Szucs and Ungerleider[8] found rheumatic fever patients with normal AV conduction time in whom they were able to distinctly prolong the PR interval by pressure on the right or left carotid sinus. This effect was best obtained with the patient in the upright position. The likelihood of a positive response was greater when the left side was stimulated. A preliminary subcutaneous injection of 0.5 mg. of prostigmine augmented the response to carotid sinus pressure. These effects were not obtained on a group of controls.

An analogous procedure, utilizing injections of ergotamine tartrate, which enhances vagal action, has been demonstrated by Wendkos.[26]

Another procedure, already mentioned but deserving reemphasis, for the detection of cardiac involvement in rheumatic fever, is the taking of frequently repeated electrocardiograms. By this practice, the normal for the individual is established and transient changes are more readily observed.

The use of multiple precordial leads in rheumatic fever may be expected to increase the proportion of positive findings in this disease as it has in other types of cardiac involvement. Wendkos and Zierler[27] have recently presented several cases illustrating this point.

THE ELECTROCARDIOGRAM IN THE DIAGNOSIS OF RHEUMATIC FEVER

As has already been pointed out, the electrocardiographic changes in rheumatic fever are not specific for this disease, but can be duplicated by a variety of diseases and circumstances. Hence, although the heart is more commonly involved in rheumatic fever than in any other common febrile disturbance, a certain amount of caution is necessary in drawing conclusions from electrocardiographic changes.

Some of the circumstances and diseases other than rheumatic fever in which electrocardiographic changes have been demonstrated and which might at times create difficulties in diagnosis will be considered.

In recent studies on large groups of healthy young people, gross deviations from accepted normal values in the electrocardiogram were demonstrated.[6,23] Graybiel and his associates[6] found the PR interval between 0.21 and 0.28 seconds in 16 of 1,000 healthy young aviators, an incidence of 1.6 per cent. Special cardiologic study in these variants failed to yield evidence of disease. In this same study, the authors found 27 men with a QRS of 0.11 seconds instead of below the accepted upper limit of normal 0.10 seconds, and 11 with a QRS of 0.12 seconds or higher.

Displacement of the ST segment more than 1 mm. above or below the base line, considered the normal range, occurred in a sizable group; and inversion of the T wave in other than the third limb lead occurred three times.

Variations from what is considered the normal electrocardiograms have been described in healthy individuals with change of posture.[14] Intense emotional stress has produced distinct electrocardiographic alterations.[12,13,28] Smoking, for a short time after its performance, has been shown to cause definite, though transient, electrocardiographic changes.[7,20]

Drugs, such as digitalis, quinine and atabrine, which alter the electrocardiogram might at times create confusion.

Some of the febrile diseases which may at times resemble certain expressions of the rheumatic fever state and which have at times been found to be accompanied by electrocardiographic changes are influenza,[9] atypical pneumonia,[17] tuberculosis,[15] typhoid fever,[18] infectious mononucleosis,[4] and disseminated lupus erythematosus.[15] Some of the arthritides are, in some circumstances, most difficult to distinguish from rheumatic fever. For example, rheumatoid arthritis and gonorrheal arthritis are not infrequently associated with electrocardiographic defects.[15,16]

The aforementioned entities, which may, by their clinical and electrocardiographic aspects, simulate phases of the rheumatic fever state, and thus possibly make diagnosis difficult, seem like a formidable array. Nevertheless, the practitioner may be comforted by the fact that in most cases of rheumatic fever the diagnosis is readily apparent on clinical grounds, and that the electrocardiogram is altered so much more frequently in rheumatic fever than in most diseases which might simulate it, that the presence of a distinct change in the electrocardiogram may be looked upon as a point indicative of this disease.

SUMMARY

The important electrocardiographic changes in rheumatic fever have been enumerated.

Some of the mechanisms of their production have been discussed.

A few procedures to increase the value of the electrocardiogram in the diagnosis and observation of rheumatic fever have been touched upon.

Some of the diagnostic problems related to the use of the electrocardiograph in rheumatic fever have been mentioned.

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CASE REPORTS

- Aphthous Oral and Genital Ulcers With Conjunctivitis (Behcet's Triple Symptom Complex)
- Carcinoid of the Appendix, Simulating Closely Primary Carcinoma of the Appendix
- Disseminated Coccidioidomycosis: Isolation of Causative Organism from the Urine
- Urethral Diverticulum With Calculi in Women

Aphthous Oral and Genital Ulcers With Conjunctivitis (Behcet's Triple Symptom Complex)

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ALTHOUGH others had previously reported similar cases, Behcet[1] is generally credited with first recognizing the interrelationship of the symptoms comprising what he termed the triple symptom complex. Curth[2] has brought the subject up to date in an excellent article published in 1946. The following case is reported because of the complete investigation which the patient received in three institutions and because of the apparent rarity of the condition.

A 17-year-old male, native of California, was admitted to Santa Barbara Cottage Hospital January 15, 1947. He developed "canker sores" in 1945. These lesions became progressively more severe and were quite painful. He was unaware of any blisters at any time. He had been free of lesions at intervals but in the free intervals had had a redness of the throat. In an auto accident in the fall of 1945 he received a laceration of the right eye and of the forehead and nose. He was given sulfonamides and hyperpyrexia at that time and was free of oral lesions for some time thereafter. However, the lesions reappeared and progressed. He was twice hospitalized elsewhere* for this condition and was very thoroughly investigated. In August, 1946, perianal lesions appeared, and in September, 1946, scrotal lesions appeared. In mid-September, an abscess developed about a foreign body in the nose, and the patient was hospitalized, the abscess drained and penicillin administered. The scrotal lesions became much worse during this time, and he was confined to bed most of the time from then until he came under our observation.

The patient had had the usual diseases of childhood. He had lesions described by his father as blisters around the mouth, beginning when the patient was nine months of age and persisting for an unspecified period. At fifteen months of age he developed asthma, which persisted into his sixteenth year. Tonsillectomy was performed at age five. An appendectomy was followed by phlebitis at age 12. At age 12 he also suffered from a severe sore throat which lasted for three weeks. He was run over by a tractor with resultant injury to the shoulder girdle at age 13, suffered a severe burn of the back at age 14, and had an injury of the nose, followed by infection, at age 15. The infection was treated with penicillin.

The patient has been hospitalized five times at the Cottage Hospital and once at a Mid-west clinic† since he came under our observation. When first seen January 15, 1947, he weighed 110 pounds, a loss of 27 pounds from his best weight. He presented partial baldness of the borders of the tongue. On the right lower lip was a heavily crusted ulcer. The nasopharynx was partially denuded and whitish as though there was a great deal of underlying scar tissue. At the base of the penis and extending on down to the scrotum and the right perineum was a heavily crusted, foul smelling, deep ulcer, with rolled borders. The base was covered with thick creamy pus. Aside from the laceration of the right eye, the eyes appeared normal. The temperature was normal upon admission and remained so throughout all the hospitalization, except when fever was induced.

Extent of ulceration during most recent hospitalization.

While the patient has been under our observation the lesions have been present intermittently and have become increasingly severe. There has been some hemorrhage from the lesions at times.

Injection of the left cornea was noted in January of 1947, at which time repeated questioning brought out that there had been mild injection of the cornea at intervals for some time. He continued to have occasional corneal injection. In September, 1947, the right lid margins became thickened and crusted. Vision had not been impaired at any time (other than from the old injury to the right eye). Late in 1947 the patient first noted photophobia. In May, 1947, he noted a blister over the left deltoid. This blister broke, resulting in a typical ulcer. He also developed pustules followed by ulcers at the sites of therapeutic smallpox injections and some of the skin tests in late 1947. About the same time he noted blisters on the toes. These blisters healed without destroying the skin, and none were present when he was under our direct observation. Eye examination in March, 1947, showed the left retina to be essentially

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*Robert C. McNaught, M.D., provided a resume of the patient's record at Stanford University Hospital.

†Robert R. Kierland, M.D., provided a resume of the patient's record at The Mayo Clinic.

normal. The conjunctiva was pale and somewhat edematous at the fornices. The right eye could not be examined because of the old injury. He was followed during December, 1947, by an ophthalmologist. At no time was iritis found. The left optic disc arterioles and venules were normal in color and contour. There was one small, pinhead-sized, dull black pigment speck adjacent to the inferior temporal vessels 6 disc diameters out from the disc. Elsewhere about this area and in other areas the extreme periphery was somewhat more pigmented than one would expect in this type of fundus; however, this pigmentation was not a pattern which could be identified as any pathological process at that time.

Laboratory: The reports from all three institutions in which this patient was hospitalized were made available to us and will be presented together. Results of histoplasmin and coccidioidin tests were negative in June, 1946, and September, 1947. Tuberculin test 1-10,000 was negative as was the Frei test. Moderate anemia was usually present 10.5-13 gm. (64 per cent-84 per cent). The patient often had a relative neutropenia (as low as 51 per cent) with an occasional moderate leukocytosis up to 12,500 per cubic millimeter. Serologic tests for syphilis were negative. Roentgen examinations of the chest revealed no abnormalities. Blood culture was negative. Cultures from the lesions showed various organisms at various times. Staphylococci and green-producing streptococci as well as proteus vulgaris were found. At one time coagulase-positive, pigment-producing hemolytic staphylococcus aureus was found in the eye and in the nasopharynx. Fungi and tubercle bacilli could not be cultured. Stool culture showed no members of the typhoid or paratyphoid group. Undulant fever agglutinations were positive 1:20 through 1:320 upon one occasion but were subsequently negative. There was no reaction when brucellin was administered intramuscularly. Repeated urinalyses were normal except for a few hyaline and granular casts upon one occasion and a slight trace of albumin upon another occasion. Darkfield examinations of the exudate from the lesions showed no spirochetes. The seventeen ketosteroids were reported as 5.2 mg. per 24 hours. Blood, biopsy specimens, curettings from the ulcer base, stool specimens, smears from the ulcers, and paraffin sections were examined for virus‡ The sections were stained with eosin-methylene-blue. The smears were stained with Giemsa, Macchiavello's stain and methylene blue. None of the material examined showed any evidence of inclusion bodies, either cystoplasmic or intranuclear. No immune bodies for herpes simplex were demonstrated in the blood serum by a simple neutralization test in mice.

The biopsy specimen and some of the whole blood were inoculated intracerebrally into six-day unweaned mice. Some of the animals were sacrificed at the end of one week, the rest at the end of two weeks, and material passed on to another set of six-day mice. These were observed for one month. Adult mice were also inoculated with biopsy material and carried for three passages. The curettings and stool specimens were inoculated into young rabbits by scarifying the corneas. Some of the biopsy material was inoculated to the chorio-allantoic membrane of ten-day chick embryos but was not carried beyond the second passage because of difficulty with bacterial contamination which persisted in spite of the use of penicillin and streptomycin. Biopsy material (which had been stored in dry ice for two weeks) was inoculated into hamsters. In all respects, the specimens were completely negative for virus material that could be transmitted to laboratory animals.

‡Virus investigations were performed by Peter L. Beal, M.D.

TREATMENT

Local therapy, including tyrothricin, permanganate, and dilute acetic acid was ineffectual. The lesions progressed in spite of systemic treatment with streptomycin, penicillin, blood transfusion, the sulfonamides, folic acid, protein hydrolysate and vitamin supplements. The patient was also subjected to numerous bouts of hyperpyrexia by means of triple typhoid vaccine and the Kettering hypertherm. Benadryl, crude liver extract, testosterone, and repeated intracutaneous injections of smallpox vaccine were also tried. Exacerbations and relapses occurred in spite of all treatment, although it was our opinion that, for a considerable time, the severity and the duration of the attacks were materially lessened by the use of triple typhoid hyperpyrexia. Such therapy was without effect, however, during the most recent hospitalization.

DISCUSSION

In the case under consideration, the following conditions were considered in differential diagnosis:

1. Erythema multiforme of the ectodermosis erosive pluriorificialis type. This condition is primarily a vesicular and bullous disease which usually has an acute onset with fever and constitutional symptoms. It usually runs its course in from three to six weeks. Relapses occur but are not the rule.

2. Pemphigus: The age of the patient and the lack of true bullae ruled against this condition. Pemphigus vulgaris does not involve the eye and no type of pemphigus results in such ulcers as this patient presents.

3. Dermatitis medicamentosa: The medication which this patient takes has been known and followed for a prolonged period of time.

4. Aphthous fever: (foot and mouth disease). This condition, which is self-limiting and primarily a vesicular disease, was ruled out by the history, as well as by the recurrent attacks which the patient suffered.

5. Periadenitis mucosa necrotica recurrens (ulcus neuroticum mucosae oris). This disorder is described as beginning with smooth, red, hard nodules which slough out a solid, mummified plug leaving a crateriform depression which heals in five to eight days. Fordyce[5] has seen this condition on the vaginal mucosa. It may be that some of the cases described under the above title belong to the group known as triple symptom complex or vice versa, but the patient under consideration did not have primary lesions as hard nodules, and plugs of tissue were not sloughed. Also, the lesions became much larger than those described under the above title and persisted much longer.

6. Aphthous ulcers: Touraine[7] has suggested that aphthous ulcers, triple symptom complex, periadenitis mucosa necrotica recurrens, ulcus vulvae acutum, and several similar conditions be classed as members of one group, the aphthoses. On a clinical basis alone, it would be impossible to differentiate the lesions of the less severe cases of triple symptom complex from those of the more severe cases of aphthous ulcers. The lesions presented by this patient were more severe than those usually termed aphthous ulcers, but there was no way of proving that he did not have aphthous ulcers. Laboratory tests did not clarify the diagnosis.

7. Ulcus vulvae acutum: Ephraim[4] states that this condition has been seen on the scrotum, root of the penis and on the buttocks. What has been said about aphthous ulcers also applies to this condition. Oral lesions sometimes accompany ulcus vulvae acutum. The presence of bacillus crassus in the lesions would favor a diagnosis of ulcus vul-

vae acutum, but there is reasonable doubt that these organisms have any causal relationship to the condition. These organisms were present in Curth's second case.[3]

After considering the above conditions, this patient was thought to have the triple symptom complex as described by Behcet[1] because of the insidious onset, the type and location of the lesions, the recalcitrance to all forms of therapy, the conjunctivitis, and the formation of pustules at the sites of skin abrasions from intracutaneous and subcutaneous injections. Iritis leading eventually to hypopion is the usually described eye condition associated with triple symptom complex. The diagnosis in the case presented might be challenged since only conjunctivitis was present. However, Behcet[2] points out that eye lesions may not be present and Franceschetti and his coworkers[6] state that the first sign of eye involvement may be photophobia and irritation of the ball, and that iritis and hypopion may develop only very late in the disease. Moreover, the skin manifestations are usually, but not always, present for some time before any eye symptoms appear. Since iritis is a manifestation of disease elsewhere in the body, it is not surprising that it sometimes develops in association with these chronic recurrent ulcers.

The ophthalmologist who observed the patient suggested that the eye picture in the case being presented might be due to contamination from the oral and genital lesions. That theory was partially borne out by the finding of identical pigment-producing, coagulase-positive staphylococci in the nasopharynx and in the eye. However, these organisms were found in the eye but once. Only time will tell what picture the uninjured eye will eventually develop.

The extensive laboratory investigations to which this patient was subjected revealed nothing relative to the cause. The low seventeen ketosteroids had not been previously found, but therapy in the form of testosterone did not result in any improvement; this finding probably had nothing to do with the skin picture. The investigations of one set of samples for viruses were negative as were similar investigations reported by Curth.[3] The elementary bodies described by Behcet[2] were not found. Aside from streptomycin, testosterone, and tyrothricin, all therapy used on our patient had been tried previously on patients with this condition.

SUMMARY

The case of a 17-year-old white male who has recurrent painful ulcers of the oral cavity and genitalia, as well as recurrent conjunctivitis, is presented. This patient is thought to have the triple symptom complex described by Behcet. No cause was found for the condition and no treatment has appreciably influenced the course of the disease.

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Carcinoid of the Appendix, Simulating Closely Primary Carcinoma of the Appendix

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THIS is the report of a case of carcinoid of the appendix that closely simulated primary carcinoma of the appendix. This case was somewhat unusual in that there was a history typical of recurrent attacks of acute appendicitis of ten years' duration, and some of the attacks had been quite severe. One month before the patient was operated on, she had a moderately severe attack. She wanted to postpone operation, if possible, for a month or two, when she could have a uterine suspension, ovarian cystectomy, and conization of the cervix, as well as the appendectomy.

Both Foot and Boyd intimate that carcinoid tumors are usually found at operations for other conditions than disease of the appendix, or at necropsy. Carcinoid tumor of the appendix is found in 0.3 to 0.4 per cent of appendices removed surgically, according to Boyd. This condition has been described in the literature as primary carcinoma of the appendix, and the case here reported was originally thought to be one of primary carcinoma. Five pathologists, however, were of the opinion that the tumor was carcinoid.

True adenocarcinoma of the appendix is extremely rare. Boyd states the histological picture suggests carcinoma, while the clinical course is usually that of a benign lesion. In 90 per cent of the cases the lesion is situated near the tip of the appendix. The appendix is usually not elongated, but may be broader than usual, and firm. A membrane may be present on the surface. Cross-section reveals a yellow ring which encircles the appendix and appears to be situated in the submucous coat. This is due to a lipoid material. Microscopically the tumor consists of spheroidal cells, arranged in very definite groups or masses suggestive of a carcinoma, and although never showing a true gland-like arrangement, sometimes the cells may be grouped around a rather atypical and irregular lumen, as they were in this case. Although usually confined to the mucous and submucous coats, the cells may penetrate the muscularis, and even the subserous coat, as they did in this case.

Carcinoid tumors may be found in any part of the gastrointestinal tract, although most frequently in the small intestine, where they are often multiple. In the appendix they are always single.

CASE REPORT

The patient, a 37-year-old white married woman, was first observed February 3, 1947, because of steady, dull pain of three days' duration in the right lower quadrant of the abdomen. There had been some nausea but no vomiting. Bowel movements were normal. Past history revealed recurrent episodes of similar distress over a period of ten years. The patient had also had considerable dysmenorrhea since puberty, and had had considerable low back pain in the preceding five years. There was a persistent vaginal discharge which had begun three years previously. The patient was well developed and well nourished and was not acutely ill. The temperature was 99.6° F., the pulse rate 86, and the blood pressure 120 mm. of mercury systolic and 80 mm. diastolic. Heart and lungs were normal. The abdomen was flat with slight rigidity and moderate tenderness in the right lower quadrant and there was slight rebound tenderness. Rectal examination disclosed no abnormality. Upon examination of the pelvis the cervix was found to be moderately eroded and everted, and the uterus was retroverted. There was a cyst measuring 3 x 4 cm. in the left ovary, which was tender. The right adnexial region was moderately tender.

Examination of the blood showed hemoglobin 88 per cent (15 gm. per 100 cc.). Erythrocytes numbered 4.3 million and leukocytes 10,300 with normal distribution of polymorphonuclear cells, lymphocytes, stabs, segmented cells and monocytes. A Wassermann test of the blood was negative. Urinalysis was normal.

The diagnosis of recurrent appendicitis was made and the patient was observed closely. On February 26, 1947, she was operated upon. The appendix, which was elongated and moderately broad, lay retrocecal and was completely bound down to the posterior surface of the cecum by dense adhesions. It was surrounded by moderate inflammatory reaction. The uterus was retroverted and there was moderate relaxation of the supporting ligaments. A cyst measuring 3 x 4 x 3 cm. was found in the left ovary. The cervix was moderately eroded and everted.

Operation consisted of uterine suspension, ovarian cystectomy, appendectomy, and conization of the cervix.

Pathological Report: The appendix was 5 cm. in length and 0.7 cm. in thickness at each end. In the distal third there was a localized fusiform swelling involving the entire appendiceal wall and measuring 1.2 cm. in thickness. At the swelling the wall was yellow, the lumen being obliterated by firm, yellow-white mucoid-appearing material. Microscopic examination of sections showed the serosal surface to be intact. It was covered with flattened spindle-shaped cells. The subserosal connective tissue was sparse but in some areas contained dilated blood vessels engorged with blood. Longitudinal and circular muscular coats were well defined, but the mucosa was totally altered by the presence of a tumor made up of large, rounded islands of cells. Between these islands were elongated, irregularly shaped strands and columns of tumor cells packed fairly closely together and infiltrating the stroma without limits. These cells had invaded the muscular walls in many places, and in one area were present in the subserosal connective tissue adjacent to the serosa. Wherever seen the cells were similar in character, being fairly small and round, with scanty cytoplasm and round to ovoid nuclei which were dark staining, with discrete nuclear membranes and dusty particles of chromatin material dispersed throughout the nucleus. Some contained fairly well defined, slightly irregularly outlined nucleoli in their central portions. Mitotic figures were not observed.

Diagnosis: Argentaffinoma (carcinoid), appendix.

The patient made a very satisfactory recovery and was dismissed from the hospital on the sixth postoperative day. Examined every two months since leaving the hospital, she has had no complaints other than of an occasional pain in the right lower quadrant, where slight tenderness has persisted. Otherwise the abdomen appears to be normal.

COMMENT

These rare tumors of the appendix are of interest to the surgeon because of the differential diagnosis, and because they may be the source of a metastatic lesion, the treatment of which may be somewhat of a problem, with necessity for fairly close observation of the patient for many years. The great majority of the patients are completely cured by removal of the carcinoid tumor.

As a rule a carcinoid tumor behaves in a benign manner, although it may infiltrate the wall of the appendix. It may, however, metastasize to the regional lymph nodes and also to the liver. Metastasis is more likely to occur from a carcinoid tumor in the small intestine than from one arising in the appendix. Metastases are, however, always slow to occur and slow to cause termination. Boyd states metastatic lesions have been found as late as 20 years after a carcinoid tumor was removed.

Many of the cells of a carcinoid tumor contain granules which stain black with silver salts (argentaffin) and yellow with chromium salts (chromaffin). A relationship exists between carcinoid tumors and argentaffin-cell neuromas. Apparently the paraganglionic cells in the plexus of Meissner and Auerback have something to do with the origin of the tumor. Some believe that this may be the origin of the so-called "neurogenic appendix."

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Disseminated Coccidioidomycosis: Isolation of Causative Organism from the Urine

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IN the case of disseminated coccidioidomycosis which is reported here, a very unusual feature occurred which, to the best knowledge of the authors, has never been reported previously.

CASE REPORT

A 27-year-old negro male was admitted to the Oakland Veterans Administration Hospital January 28, 1947. The patient was born and reared in Paris, Texas. He served in the Army from February, 1942, to August, 1944, most of the time in Louisiana. He had no overseas service. The past history was negative except for syphilis contracted in 1942 and treated for six months with mapharsen and bismuth with subsequent negative results of blood and spinal fluid examinations. A review of Army medical records revealed repeatedly negative chest roentgenograms. Upon release from the military service the patient came to Oakland, California. In the latter part of 1946 he moved to Madera, California (located in the San Joaquin Valley), where he worked as a crop picker up to the time of the present illness which began December 1, 1946, with chills, fever, cough, and right chest pain. He was treated at a local hospital for right lower lobe pneumonia with penicillin and was discharged January 1, 1947. He continued to feel weak, and had a cough productive of small amounts of green sputum. On admission to the Oakland Veterans Administration Hospital the temperature was 102° F., pulse rate 110, respirations 24 per minute and blood pressure 100 mm. of mercury systolic, 60 mm. diastolic. The patient appeared acutely ill and showed evidence of considerable weight loss (height 73 inches, present weight 135 pounds, average weight 152 pounds). No palpable lymph nodes were present. The lungs were clear to percussion and auscultation and the remainder of the physical examination was negative. The routine and follow-up laboratory data are shown in Table 1. The Kahn test of the blood was negative. The blood urea nitrogen was 12 mg. per 100 cc. A roentgenogram of the chest, taken on admission, was reported as follows: "The cardiac shadow appears normal. Both lung roots are moderately prominent and there are some faint exudations in the right mid-lung field with an area 1 cm. in diameter which may represent a cavity. On

From the Medical Service, Oakland Veterans' Hospital.

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TABLE 1.—*Results of Sputum, Urine and Blood Examinations for Coccidioides*

Date	RBC (Million)	Hgb. (Gm.)	WBC	Sed. Rate mm./hour	Urine Sediment (cells/ h.p.f.)	Urine Culture	Sputum	Tbl. Skin Test	Coccidioides Skin Test	Coccidioides Compl. Fixation	Blood Culture
Jan. 28	3.65	10.9	9,200	119	1- 3 RBC	.....	Neg.	.....	.....	.....	.....
Feb. 1	.....	.....	.....	.....	8-10 RBC	.....	Neg.	.....	.....	.....	.....
Feb. 3	.....	.....	.....	.....	.....	.....	Neg.	1:1000 Neg.	1:1000 Neg.	.....	.....
Feb. 10	3.6	10.6	13,600	.....	.....	.....	Neg.	.....	.....	.....	.....
Feb. 14	2.85	9.4	8,600	.....	.....	.....	Neg.	.....	.....	.....	Neg.
Feb. 22	.....	.....	.....	.....	.....	.....	.....	.....	1:100 Neg.	.....	.....
Feb. 24	.....	.....	.....	.....	.....	.....	.....	.....	.....	++++1:128 +1:256†	.....
Mar. 3	.....	.....	.....	.....	.....	.....	+C. immitis	.....	.....	.....	.....
Mar. 13	.....	.....	.....	.....	.....	.....	.....	.....	1:10 Neg.	.....	.....
Mar. 14	2.65	8.6	24,600	.....	Loaded RBC	+C. immitis*	.....	.....	.....	.....	.....
Mar. 17	.....	.....	.....	.....	.....	.....	.....	.....	Undil. Neg.	.....	.....
Mar. 21	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	+C. immitis

*Positive cultures both at Oakland Veterans Administration Hospital and at Stanford University Laboratory.
†Facilities of the coccidioidomycosis study, Commission on Acute Respiratory Diseases, Army Epidemiological Board at Stanford Medical School.

lateral projection these are seen to lie posteriorly in the upper portion of the right lower lobe." Subsequent roentgenograms of the chest on February 12 and February 24 showed no essential change.

The patient had a temperature ranging daily from 99° F. to 104° F. during the entire period of hospitalization.

On February 17 a firm and non-tender small lymph node was noted at the angle of the right mandible. This was removed for biopsy and the pathological report was as follows: "The specimen consists of a firm, irregular mass 18 x 18 x 15 mm., the outer surface of which has numerous connective tissue tags and small fat lobules. The cut surface shows considerable variation in configuration, some areas being firm, white, and semi-translucent and others opaque and hemorrhagic. Microscopically, the lymph node contains numerous localized areas of granulomatous structure in which there is moderate central necrosis, an outer zone of lymphoid tissue, and an intermediate zone of increased epithelioid formation. Among the latter there are numerous giant cells. Scattered throughout the granulomata there are numerous large double-walled structures containing numerous endospores. In addition there are many small isolated endospores characteristic of Coccidioides."

Results of sputum, urine, and blood examinations for Coccidioides are shown in Table 1. On March 4 the patient developed tenderness over the mid-sternal region. Enlarged lymph nodes appeared in the right axilla. By March 10 a definitely fluctuant mass had developed in the mid-sternum opposite the third rib. However, roentgenograms of the sternum taken at this time were normal. X-ray films of the thoracic and lumbar segments of the spine, knees, ankles, and abdomen, were all reported as negative. As no specific treatment for disseminated coccidioidomycosis is known, vaccine treatment was attempted although little hope was held for benefit. The patient also received repeated blood transfusions, but the course was progressively downhill and he died March 22, 1947.

POSTMORTEM EXAMINATION

The body was that of an undernourished, slender, negro male, measuring 6 feet 3 inches in length, and estimated to weigh approximately 100 pounds. There was a soft fluctuant mass just below the xiphoid, which, on palpation, had some bony crepitation. There was a second small fluctuant mass over the xiphoid process. Each was approximately 4 cm. in diameter. There was considerable wasting of the soft tissues.

Subcutaneous fat was negligible. The lower border of the liver was 4 cm. below the costal margin. The two small fluctuant masses on the sternum were found to be abscesses filled with thick, green, purulent exudate. Smears showed typical Coccidioides spherules. In each instance the bone was eroded. The upper lesion had completely destroyed the bone on both sides of the sternum, but had not perforated the soft tissues on either side. The lower lesion involved only the anterior table of the sternal structure.

Heart: The heart weighed 250 gm. A few small, pinpoint, white tubercles were seen through the pericardial surface. Similar depositions were observed in the myocardium and shining through the endocardium. These were minute and sparse. The muscle was pale but firm.

The right lung weighed 1,500 gm., the left 1,250 gm. The pleural surfaces were smooth, but shining through the pleura on either side were innumerable small white tubercles. The tissue, the consistency of liver, was readily cut, and innumerable small tubercles were observed on the sectioned surfaces, in all portions of the lung. There was no evidence of bronchial distribution of the tubercles, but no portion of the lung had escaped. The major bronchi did not contain exudate, and no localized abscesses were seen in the pulmonary tissues. The mediastinal lymph nodes were enlarged, particularly those in the upper portion of the mediastinum anteriorly. One of the nodes in this region was sectioned, and considerable purulent fluid exuded into

the pleural cavity. Other abscesses were found in the lymph node chain extending from the extreme upper limits of the mediastinum down to the diaphragm. The largest of these nodes was approximately 3 cm. in its greatest diameter.

Liver: The liver weighed 1950 gm. The border was rounded and the surface slightly nodular and rough, with the gross appearance of cirrhotic liver. The sectioned surface everted moderately, was resistant to cutting and appeared to be cirrhotic. In addition, there were small white, discrete tubercles scattered throughout all sectioned surfaces. The gallbladder and bile ducts appeared to be normal.

Spleen: The spleen weighed 240 gm. It was pale in color, the borders were rounded, and the tissue was moderately flabby. On the sectioned surface, as well as shining through the peritoneal surface, there were many small white tubercles. The sectioned surface everted moderately, and in several areas there were localized accumulations of thick, green pus in abscesses approximately 6 mm. in diameter.

Pancreas: The pancreas was normal in size and shape. Along the upper border of the pancreas, in the line of blood vessel drainage from the spleen toward the celiac axis, there was a group of enlarged lymph nodes, some of which contained a large amount of greenish exudate. This chain of nodes extended from the tail to the head of the pancreas.

Adrenals: The adrenals were normal in size, color, and consistency. In one adrenal in the medullary portion there was an aggregation of gray material.

Genito-Urinary Tract: The right kidney weighed 270 gm., the left 250 gm. The sectioned surface everted moderately, and was pale in color, but the line of demarcation between cortex and medulla was sharp. Studded throughout the parenchyma in both cortex and medulla were numerous small, white aggregations of material. No exudative material was found. The pelves and ureters were normal-appearing, as were the bladder, prostate, and external genitals.

Vertebral Column: There were accumulations of fluctuant masses adjacent to the bodies of the vertebrae from the seventh dorsal to the first lumbar. These were most numerous along the left side, and in four distinct areas the purulent exudate was in direct continuity with the cancellous portions of the bodies of the vertebrae. There was such an abscessed cavity on both sides of the 11th dorsal vertebrae. No evidence of extension of the exudate into the psoas muscle sheath was demonstrated.

Central Nervous System: The convolutions of the brain were normal in size and the sulci were not broad. There was no evidence of meningeal exudate or localized deposition of inflammatory material. The surface of the brain was washed and carefully examined, but no evidence of "tubercles" could be seen. The base of the brain was particularly examined, but no pathologic changes were recognized grossly.

Microscopic Examination: Microscopic examination of the lungs, heart, liver, spleen, pancreas and adjacent lymph nodes, adrenals, kidneys, subcutaneous tissue and central nervous system revealed inflammatory changes with spherules characteristic of Coccidioides.

DISCUSSION

The patient's place of residence immediately made coccidioidomycosis a consideration in diagnosis, but with the subsequent negative skin tests, adenopathy, and urinary findings, a lymphoma was considered a much more likely possibility. However, with the pathological report of the lymph node biopsy all investigative procedures were turned toward the study of coccidioidomycosis. This resulted in the finding of a positive complement-fixation and in the subsequent recovery of the organisms from the sputum, the urine, and terminally from the blood stream. It is not too uncommon to recover C. immitis in blood cultures taken within 24 hours of death in cases of disseminated coccidioidomycosis. However, it is definitely rare to find the organisms in the urine. To the best knowledge of the authors this has never been reported in the literature. The physician who examined the urine had never before isolated the fungus in the urine.*

SUMMARY

1. A case of disseminated coccidioidomycosis is presented with involvement of the lungs, lymph nodes, bone, liver, spleen, kidneys, heart, adrenals, and brain.

2. C. immitis was cultured from the sputum and urine during the course of the patient's hospitalization. A blood culture within 24 hours of death was also positive.

3. The unusual feature of this case, which is believed to be unreported previously, is the identification of C. immitis in the urine.

*C. E. Smith: Personal communication.

Urethral Diverticulum with Calculi in Women

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CALCULI complicating urethral diverticulum in women is rare, approximately 40 such cases having been reported. The case here reported is that of a woman aged 47 years with such a condition producing typical local symptoms and recurrent cystitis.

ETIOLOGY

The following, adapted from Johnson,[3] summarizes the present concept of etiology.

Acquired	Congenital
1. Trauma of childbirth	1. Gärtner's duct
2. Infection of urethral glands with sealing off of opening to urethra, formation of abscess and reestablishment of communication	2. Cysts formed from faulty union of primal folds
3. Instrumentation of urethra, especially deep fulguration of urethral lesions.	3. Cell rests
4. Secondary to urethral stricture	4. Wolffian duct
5. Secondary to urethral stone	5. Vaginal cysts

Johnson personally believed the majority of diverticula to be congenital in origin, either present in situ as such, or developing from congenital cysts which acquire an opening into the urethra by trauma or infection, or from infected glands of the middle third of the urethra which are there as an anomaly, according to Cabot and Shoemaker.[1] However, in regard to the last possibility, Lintgen and Herbut[5] in examination of 100 female adult urethras found glands in every case in the anterior urethra and in 65 per cent of the posterior female urethras. This would suggest that infected

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glands may be the most common cause of diverticula. Menville and Mitchell[6] agree with this theory.

The probable sequence after the diverticulum is formed has been stated by Higgins and Roen[2] to be, first, infection of the urine, then a lapse of time during which the diverticulum enlarges and urinary salts precipitate in the stagnant urine, leading to calculus formation. The possibility of calculi being passed from a kidney or the bladder and lodging in a diverticulum must be considered. In the case to be reported I believe the diverticulum formed from an infected gland and that the calculi formed within the diverticulum.

SYMPTOMS

The symptoms may be local and caused by the presence of the sac and calculi, or urinary and traceable to mid- or upper urinary tract infection.

Local symptoms usually consist of (1) a vaginal mass which may partially empty with the urethral passage of pus or urine if there is room for retained urine about the calculi, (2) urethral or perineal pain, (3) painful intercourse, and (4) possibly hematuria, especially after coitus.

Urinary symptoms result from the almost inevitable infection, and the degree depends upon the upward spread and resultant pathological changes in the urinary tract. As Johnson states, these vary from "recurrent attacks of cystitis to persistent urinary infection with exacerbations of frequency, strangury, and terminal hematuria. The presence of chills, fever and backache suggest an associated pyelonephritis."

DIAGNOSIS

A typical history of local symptoms as described would strongly suggest the presence of urethral diverticulum with or without calculi. Palpation of the urethra on vaginal examination would disclose a mass on the ventral surface of the mid-urethra which might be fluctuant until urine was expressed, then hard with possible crepitation as in the case reported.

A roentgenogram of the bladder and sub-pubic area would disclose opaque calculi. The diverticulum could be demonstrated by filling the bladder with a radio-opaque medium and having the patient void against the pressure of a finger against the meatus or obstructing the bladder neck with a bag catheter and injecting the urethra through the meatus.

Urethrocystoscopy either with the right angle lens or the foroblique lens while viewing the ventral surface of urethra with the water flowing will usually allow visualization of the orifice. (This is, by the way, a good routine practice.) A urethral catheter may then be coiled in the sac and roentgenograms taken before and after the injection of an opaque medium, both in the anterior and oblique positions. Demonstration of the size and location of the sac in relation to the base of the bladder is of aid in the surgical excision, according to Kutzmann.[4]

TREATMENT

Conservative medical treatment of urethral dilatation and urethral instillations is only palliative, since infection cannot be cured by this means.

Minor surgical procedures such as enlarging the orifice of the diverticulum with an electrical loop or knife through a cystoscope may also enable one to evacuate calculi but will not cure the original cause of their formation, the diverticulum. Incision and drainage of an acutely infected diverticulum pointing into the vagina may be necessary with later repair.

Radical surgical excision of the sac and contained calcuii is the procedure of choice and usually results in cure. The procedure is first to insert a retention catheter in the bladder, which aids in visualizing the structures and in the repair of them. Then a vaginal incision is made over the sac, the vaginal mucosa dissected to each side and the sac freed by blunt or sharp dissection as may be necessary to expose the neck of the diverticulum at its junction with the urethra. The structure is then excised at this point. The urethral defect is approximated with No. 00000 chromic catgut on an atraumatic needle, the periurethral tissues with No. 00 plain catgut or fine stainless steel wire in one or two layers, and the vaginal mucosa with No. 1 chromic catgut. Antibiotics such as penicillin and streptomycin or penicillin and sulfadiazine should aid in healing by keeping the urine sterile or little infected. A vaginal pressure pack may be used for 48 hours. The catheter is left in place for seven to ten days, by which time the area is usually healed.

CASE REPORT

The patient, nullipara, aged 47 years, when first seen in January, 1948, complained of recurrent frequency and dysuria of many years' duration. In June, 1947, she noted "two lumps" in the vagina. These swellings, the patient said, enlarged intermittently, and in addition there had been generalized abdominal pains, occasional nausea and vomiting, and constipation.

Previous urologic history was that of scarlet fever at the age of ten years, followed in two weeks by generalized edema from "kidney disease." The edema cleared rapidly, the patient recalled, but after that there was always some urgency and frequency in day, voiding every one to two hours, as well as nocturia three to six times. In 1929 the patient had recurrent pain in the left flank, and a specimen taken by the catheter at that time contained pus and bacteria. There was some improvement after this, with occasional flare-ups until 1943 when symptoms increased. In 1944 a plastic operation on the left ureteropelvic juncture for congenital band obstruction was performed. This was followed by hydronephrosis and pyelonephritis for which left nephrectomy was done in January, 1946. Pyelography at that time showed the right kidney to be normal but the function was moderately decreased. The urine contained Gram-negative bacilli and one to three casts per high dry field. No albumin was present.

When examined in January, 1948, the patient was obese, 65 inches in height and weighing 195 pounds. The blood pressure was 98 mm. of mercury systolic, 68 mm. diastolic. The abdomen was diffusely tender but no rigidity or masses were noted. On the left flank there was a scar but no tenderness at the site. The urethral meatus was normal, but on the ventral surface of the mid-urethra there was a cystic swelling about 2 cm. in diameter with crepitation indicating the presence of calculi. Pressure did not evacuate fluid from the meatus.

Laboratory tests: A specimen of urine taken by catheter was cloudy, alkaline, with specific gravity of 1.018, and no albumin or sugar content. Upon microscopic examination 12 to 15 leukocytes and 4 to 5 erythrocytes per high dry field were noted, and there were many bacteria. Occasional Gram-negative bacilli, and Gram-positive cocci in clumps, were observed. A non-protein nitrogen determination of the blood done February 20, 1948, showed 27 mg. per 100 cc.

Roentgen studies: Roentgenograms of the kidney, ureters and bladder and an intravenous urogram done November 20, 1947, disclosed two small densities behind the pubic symphysis, the larger 1.5 cm. in diameter and the smaller 1 cm. (Figure 1). The upper right urinary tract, faintly visualized, was grossly normal. In a urethrogram January 22, 1948, the dye outlined a 2.5 cm. diverticulum arising from the floor of the mid-urethra and containing previously described densities. A cystogram at the same time was normal. (See Figures 2 and 3.) A gall bladder and gastro-intestinal series done in October, 1947, disclosed no abnormality.

Figure 1.—Intravenous urogram, five minutes after injection, showing faintly outlined right renal pelvis with upper ureter; and two opacities just above pubis representing calculi in urethral diverticulum.

Diagnosis: 1. Diverticulum of urethra with two calculi; 2. Cystitis, chronic, mixed infection, secondary to the diverticulum; 3. Surgical absence of left kidney; 4. Hypotension, mild.

Treatment: On February 20, 1948, surgical excision of the urethral diverticulum and contained calculi was performed as described. A No. 18 (French) 5 cc. bag urethral catheter was left indwelling. A vaginal pack was inserted for pressure during the first 48 hours. Streptomycin (200 mg.) and penicillin (30,000 units) were given every three hours for three days, then every six hours for four days. Sulfadiazine, 2 gm. per day, was given subsequently.

Surgical pathology report: There was diffuse infiltration of leukocytes in the connective tissue. The mucosa was covered by transitional epithelium, with the cells considerably swollen. In the underlying stroma there was diffuse inflammatory infiltrate and in a few areas focal calcific deposits.

Two calculi, one 1.5 cm. in diameter and the other 1 cm. in diameter. They were extremely hard and the external surface was a faint greenish-gray and fairly smooth. The inner surface after splitting showed a laminated character with a whitish, softer center portion. Diagnosis: 1. Tissue consistent with diverticulum of urethra, with moderate inflammation; 2. Urethral calculi.

Postoperative course: The patient's temperature was practically normal after the operation and the urine was sterile by Gram stain to the 15th day. Despite the precautions enumerated, when the catheter was removed on the 11th day after operation there was a small fistula in the mid-portion of the repair. The urethral catheter was replaced for two weeks and the fistula progressively decreased in size. Reexamination early in April, 1948, six weeks after operation, showed almost complete healing and sterile urine, with no dysuria.

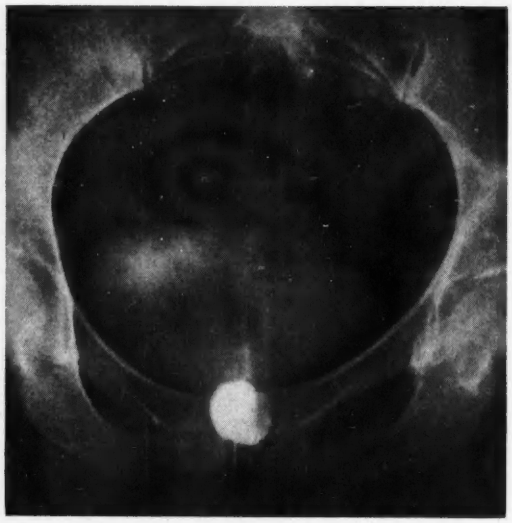

Figure 2.—Ureteral catheter in diverticulum, opaque medium injected for outline. Normal cystogram above. A.P. view.

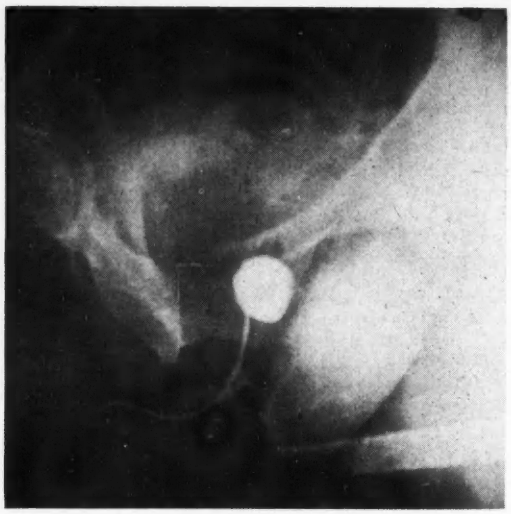

Figure 3.—Same as Figure 2 but negative shadows of calculi may be noted within diverticulum. Oblique view.

CONCLUSIONS

The origin of diverticulum of the female urethra is usually infection of urethral glands followed by periurethral abscess and sac formation.

Calculus formation in diverticulum of the female urethra is relatively rare and usually occurs from infected urine with stagnation and precipitation of urinary salts.

Diagnosis is aided by roentgen studies including the subpubic area.

Treatment is radical excision of the sac and contained calculi with repair of structures, using fine sutures over a urethral retention catheter.

Diverticulum of the female urethra with or without calculi should be considered in the presence of any chronic or recurrent urinary infection.

A case has been reported which presents most of the typical findings of this condition.

416 North Bedford Drive.

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Discussion by HENRY A. R. KREUTZMANN, M.D., *Los Angeles*

As Dr. Zide has shown, there is at present considerable controversy in the etiology of urethral diverticulae. It is too often impossible to determine from the history or from pathological examination of the excised tissue whether the sac is acquired or congenital. Most urologists are of the opinion that there is no certain method of establishing the origin of a sac.

Contrary to Johnson's belief, it is the consensus today that most diverticulae and pseudo-diverticulae are acquired. It must be remembered that not all cases present symptoms and the diverticulae then can be found only after a thorough examination. Where the sac is small and walled off, no manifestation of such a condition may be apparent. We recall one case where a diverticulum became perceptible only during the latter months of pregnancy. It grew so large as to cause the obstetrician some concern. However, after delivery it became much smaller and the patient refused to undergo operation as she had no urinary distress.

In the past few years, cases have been reported in increasing numbers, indicating that they too frequently have been overlooked in the past. Where a diverticulum is suspected, stripping the urethra and noting an excess of foul-smelling or watery pus at the meatus may establish the diagnosis.

Dr. Zide is perfectly correct in stating that routine cystourethroscopy should be performed in every case. For examining the female urethra, we have found that the best field of view has been obtained with the panendoscope.

His excellent report reemphasizes the need to examine the female urethra thoroughly in order not to overlook any pathological condition that may be present.

California Cancer Commission Studies*
Chapters XXIV and XXV

Cancer of the Bladder

A. J. SCHOLL, M.D., *Los Angeles*

ASH, after recording 3,200 cases of epithelial tumors of the bladder in the Tumor Registry of the American Urological Association, constructed the following average case from the statistics of the Registry: The patient is a white man aged 60. The chief complaints are hematuria and dysuria. Cystoscopic examination reveals a single papillary tumor located on the posterior surface of the base of the bladder. Pathologic study reveals papillary carcinoma, grade I or II. The prognosis is repeated recurrence in spite of treatment; the patient has about one chance in three of living five years and about one chance in 25 of complete recovery.

Most of the 3,200 patients represented by these case histories have been operated upon by men skilled in diagnostic and surgical urology, men capable of carrying out the type of treatment best suited for each individual case. Under these circumstances and with these figures before us, tumor of the bladder appears as an extremely lethal disease. In large part this depressing mortality is not due to the lack of response to treatment, or the incurability of bladder tumors, but to the excessively long period of time in which the tumors were allowed to progress unmolested. In a report of over 200 cases published in 1946, it was stated that an average of 12 months elapsed from the time the patient had the first symptoms "pointing the accusing finger at his bladder" until he presented himself to the urologist for diagnosis and treatment. In a published report of 135 cases of bladder tumor seen at the Los Angeles County General Hospital, 36 were so far advanced that no satisfactory treatment could be employed and in eight cases merely palliative cystotomy was undertaken. In all of these 44 cases, almost one-third of the total entry, the patients died in the hospital.

Another interesting commentary on the usual delay in the diagnosis and treatment of these tumors is that only 112 of 658 Registry patients (18.5 per cent) came under observation when the tumor was less than 2 cm. in diameter. This delay in receiving treatment in some cases is due to the lack of understanding of the portent of the symptoms on the part of the patient. One woman had blood in the urine almost continuously for ten years from the age of 40 to 50 years. She considered this to be an unusual type of menopause and did not seek treatment until sacral metastases caused severe pain.

In a fairly large number of cases delay is due to inaction, reassurance or symptomatic treatment on the part of the physician. It is not uncommon, by any means, to see patients who received advice and medical treatment for hematuria and bladder symptoms for years before cystoscopy finally is done. In some cases a urologic examination is suggested by the physician but not insisted upon; *it should be the duty and obligation of the physician who first sees these patients to make certain that the cause of hematuria or other symptoms is immediately determined.* Early observation would also aid the examining urologist, as the best time to determine the source of the bleeding is during the first attack, while the patient is still bleeding. Delay permits the growth to increase in size and to spread to layers in the bladder wall from which metastasis readily occurs.

CLINICAL DATA

Age and sex. The age of the patient is important; young adults stand the shock of operation well, but they often have extensive growths of a high degree of malignancy. In infants and in persons more than 60 years of age, the operative mortality is very high. In the Bladder Tumor Registry, which represents the age incidence in this country, the peak is reached between the ages of 60 and 64 years. Of 921 epithelial tumors, 160 (17.4 per cent) occurred at this age period. Of the 921 registered, 61.8 per cent occurred between the ages of 50 and 69 years.

The sex incidence of bladder tumors has been well established and seldom varies in published reports. Of 902 epithelial tumors of the bladder in the Carcinoma Registry, 684 (74.3 per cent) were found in the male, 213 (23.7 per cent) in the female; in five cases the sex was not stated. It has been found that among patients under 50 years the tumor in both sexes was of high degree of malignancy in 50 per cent of the cases, whereas among the patients after the age of 50, carcinoma of low grade predominated. There seemed to be no relation between sex and grade of malignancy.

Size of tumor. The size of the tumor when first seen is related to the result at the end of five years. In one hundred and twelve of 658 Registry tumors which were less than 2 cm. in diameter when first seen, the largest percentage of five-year "cures" was obtained, namely, 34 cases (30.3 per cent). When the tumor varied from 2 to 5 cm. in diameter, 82 of 309 patients, or 26.5 per cent, survived five years. However, when the tumor was larger than 5 cm., in only 35 of 222 cases (15.8 per cent) was the growth under control for five years.

*Organized by the Editorial Committee of the California Cancer Commission.

Figure 1.—Small pedunculated papilloma, base of the bladder.

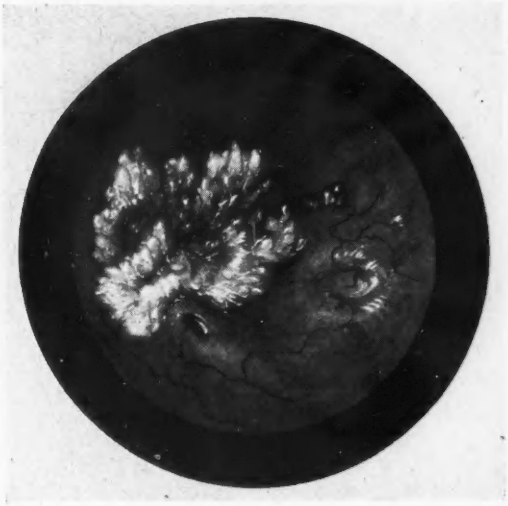

Figure 2.—Papillary carcinoma, grade II malignancy.

Location of tumor. About one-third of all tumors occur in the area of the trigone and about an equal number on the lateral walls. Ten per cent occur at the neck of the bladder and about as many on the posterior wall. A small number occur in the vault and on the anterior wall. In about 50 per cent of cases more than one area is involved.

PATHOLOGY

Practically all tumors of the bladder are epithelial in origin and may be divided into three groups; papillomas, papillary carcinomas and solid infiltrating carcinomas.

1. *Papillomas.* Simple papillomas consist of a short stalk projecting from the bladder mucosa, composed of a free, central blood supply covered with connective tissue and several layers of epithelium of adult bladder type. They vary from several mm. to 2 cm. in size (Fig. 1). *It is advisable to consider these growth not as benign lesions but as low grade epitheliomas.* Regardless of the gross or microscopic appearance many of these tumors are clinically malignant; they metastasize and recur frequently and even though early microscopic sections show no evidence of malignancy, the recurrences and metastatic deposits reveal definite malignant changes.

2. *Papillary carcinomas.* These tumors, called malignant papillomata by some pathologists, are limited in size only by the capacity of the bladder. They retain their pedicle and are composed of clubbed fronds with a marked irregularity of outline (Fig. 2). They are of a moderate degree of malignancy. In one group of 71 patients with papillary carcinoma of the bladder 26 (36.6 per cent) were dead after an average postoperative period of 11.5 months. Twenty (76.9 per cent) of those who died from malignant papillary carcinoma died in the first year after operation; 45 patients (63.3 per cent) were living an average of two years following operation.

3. *Solid carcinomas.* These tumors are of two types: the widespread papillary epithelioma, and the low, flat, infiltrating carcinoma (Fig. 3). The former has a rolled-out advancing border, the upper surface often being covered with short, stubby, papillomatous protrusions, or the top may have sloughed off, leaving a flat, ulcerated surface. These tumors, sometimes firm, are often soft, flabby and friable, and can easily be scraped off the surface of the bladder. The histological picture shows the relation of this tumor to the papilloma. In the infiltrating type the margins slope outward to meet the mucosa and burrow down into the wall of the bladder. These tumors are generally firm and compact, and without a tendency to split in cleavage planes. These solid carcinomas are the most malignant of the epithelial growths of the bladder. Sixty-seven (71.2 per cent) of a group of 94 patients with solid carcinoma were dead after an average postoperative period of 7.5 months. Fifty-nine (88 per cent) of these died the first year after operation. Twenty-seven living patients have lived an average of three years and three months.

There are a number of rarer tumors of the bladder, such as squamous cell carcinoma, adenocarcinoma, myxoma and sarcoma, which are of clinical as well as histologic interest. Benign ulcers may occur in association with infection (Figure 4).

Squamous-cell carcinomas. These tumors are distinct individual types of epithelial growths. Their onset is insidious, their growth is rapid, and they cause few distinctive symptoms. They probably develop from metaplastic bladder mucosa which has undergone epidermization as a result of irritation from infection or formation of stones. The tissue in most cases is firm and friable. The growths involve the wall of the bladder extensively, and are flat and frequently ulcerated; the lateral margins

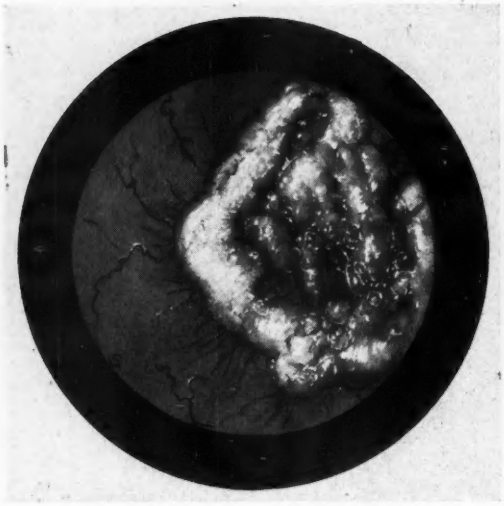

Figure 3.—Solid carcinoma in the left bladder base obstructing outlet of left ureter.

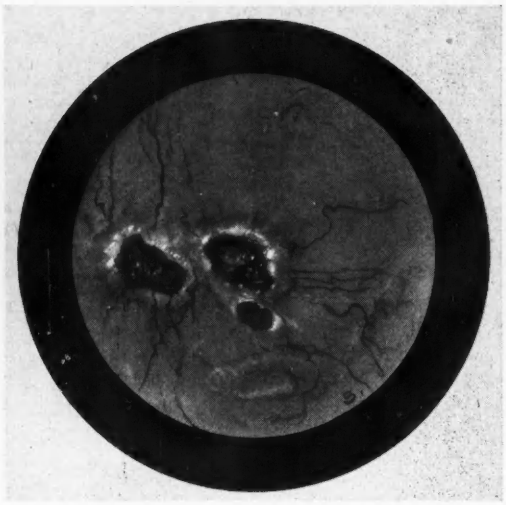

Figure 4.—Benign ulcer of bladder associated with urinary tract infection.

slope out toward the mucosa, sinking deep into the underlying tissues. Sometimes patches of leukoplakia, giving a clue to the origin of the malignancy, are found in the region of the tumor. Squamous-cell growths are most often found in early middle life and are not uncommonly preceded by evidence of long-standing cystitis. Compared with other epithelial tumors, these growths occur relatively more often in females. While metastasis is not uncommon, death in most instances is due to the obstruction and infection resulting from the local lesion. The histological examination generally shows marked cellular activity.

SYMPTOMS

Hematuria. Hematuria is the cardinal symptom of tumor of the bladder. It is the most important first signal to the patient or his doctor that a bladder tumor may be present. *It is the red flag of danger that, disregarded on first appearance, may not show a second time until the growth has progressed to a dangerous stage.*

The characteristic hematuria of tumor is spontaneous, profuse, painless and total. Tumors located near the vesical outlet may bleed slightly with onset of micturition or there may be terminal bleeding. Usually the period of bleeding is short and brisk and the interval between spells varies from days to months. This bleeding may be the sole symptom of tumor for a long time, and, as Keyes states, its very character encourages both patient and physician to pretend to themselves that the bleeding is unimportant. The tumor bleeds briefly. The patient takes a "sure" cure. The bleeding stops. It is agreed to wait to see what will happen next. A year goes by before any decision is reached —a year in which the tumor is growing, becoming larger, more difficult to control.

It is difficult to believe that of 508 cases from the carcinoma registry with initial hematuria, only half were diagnosed in the first year. Moreover, 20 per cent had to wait three years for a diagnosis and 26 cases actually were not diagnosed for seven years or more. In only one-third of these cases did the patient survive five years or more. In contrast to this surprisingly low survival in these late cases is a group of reported cases in which 142 patients with bladder tumors were cystoscoped and treated shortly after the first attack of hematuria; in all but three cases the growths were small early tumors which responded readily and favorably to treatment.

Dysuria and frequency. Painful or frequent urination is not a common accompaniment of bladder tumors, especially in the early stages of the disease. In the Registry group of cases, frequency, occurring in 15 per cent of cases at the onset of the disease, occurs in 70 per cent of cases later. This later increase is due to infection and obstruction and in some cases to extensive involvement of the bladder. In many cases there is surprisingly little bladder pain even in cases where only a small amount of bladder mucosa remains. This lack of pain is responsible for much of the procrastination in seeking treatment. Many people believe that nothing serious can occur without pain. It is not unusual to find patients who, having ignored intermittent attacks of frequency and hematuria for years, apply immediately for treatment when an extension of the growth causes pain.

DIAGNOSIS

Single or repeated attacks of spontaneous hematuria suggest the diagnosis of tumor, and the diagnosis is made by cystoscopy. Between bleedings the urine may be blood tinged or red blood cells may be found microscopically, although the absence

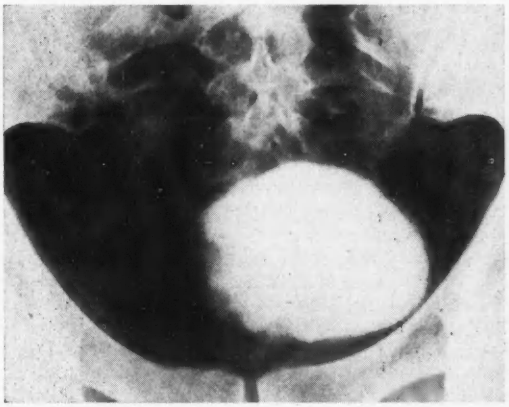

Figure 5.—Cystogram revealing comparatively small papillary tumor of right base.

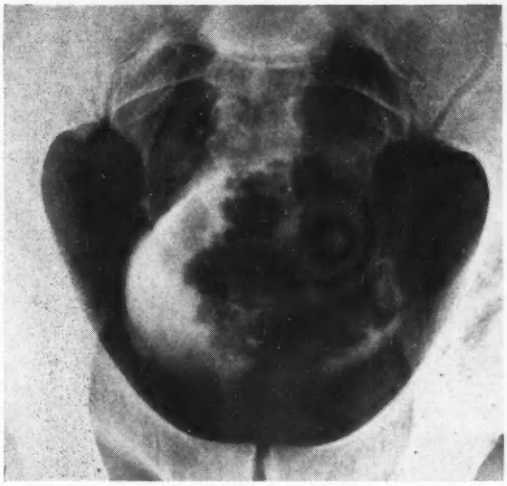

Figure 6.—Papillary carcinoma of large size. Tumor was pedunculated, of low degree of malignancy, and a good result was obtained following its removal.

of blood cells does not indicate that there is no tumor. *All patients with hematuria should be cystoscoped* by one skilled in this procedure. It is essential that the examination be painless for the examiner's sake as well as that of the patient. If there is pain with cystoscopy, not only does the patient suffer but it is also impossible for the cystoscopist to make a thorough examination. Intravenous pentothal or caudal anesthesia usually gives sufficient anesthesia for an accurate, unhurried examination. The number, size, and locations of the tumors should be noted, the base or pedicle observed and a specimen of the tumor removed for histologic examination. Cystograms are helpful in estimating the extent of vesical involvement as shown by filling defects. It may show a much more extensive involvement than would be noted by cystoscopic examination and it is also helpful in the presence of a massive pedunculated tumor when an accurate cystoscopic

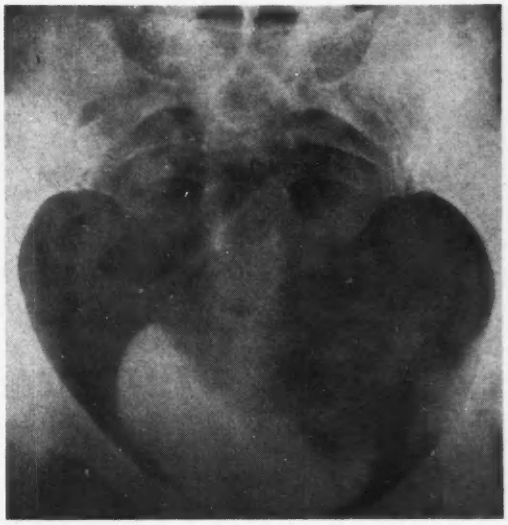

Figure 7.—Solid carcinoma covering upper third of bladder surface.

estimate cannot be made of the actual involvement of the vesical wall (Figures 5, 6, 7, 8, 9).

It is not always possible or desirable to catheterize the ureters, but some knowledge of the upper urinary tract should be obtained. This data can be obtained with an intravenous urogram which is of great help in determining the patency of the ureters and also gives a fairly accurate indication of the function of each kidney.

Hematuria in men of an age at which prostatic obstruction occurs is very commonly thought to be prostatic in origin, and on this account examination is at times delayed. One patient, an intelligent physician, aged 56, had repeated attacks of hematuria over a period of two years. He had been told the bleeding was probably prostatic, so cystoscopy was delayed. When finally it was done, there were one large papillary tumor on the lateral wall, numerous small tumors in the base and the entire prostatic urethra was filled with small papillomata.

All bladder tumors should be considered as potentially malignant. The size, location, number of tumors and the degree of penetration of the growth can be determined at the first examination. At this time a biopsy specimen should be taken.

It is not always possible by cystoscopy to determine the size of the base of the tumor or the degree of penetration into the bladder wall, for, in some cases, a tumor which appears to cover a large area of the bladder wall may be found on surgical exploration to have a small, compact pedicle. Bimanual pelvic examination should always be done, as in this way an estimate can be made of the extent of tumor infiltration especially about the bladder neck, the trigone, and the fundus.

Satisfactory equipment should be available to coagulate or treat the tumor if it is of a size to be

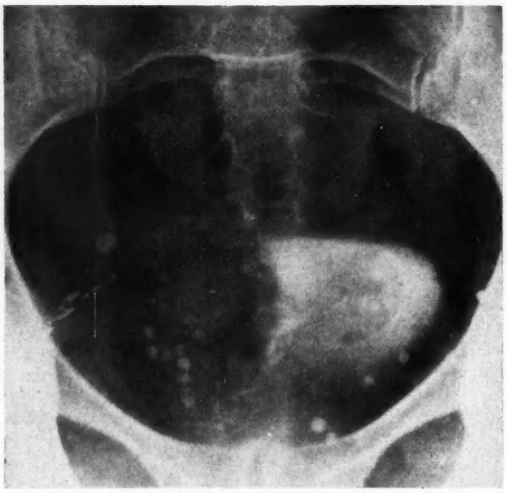

Figure 8.—Solid carcinoma of right side of bladder.

Figure 9.—Filling defect caused by hypertrophied prostate.

controlled by simple measures; if not, the required method of treatment should be decided on at this time. This is a procedure requiring considerable skill for proper performance.

TREATMENT

Collected groups of statistics indicate that treatment for tumors of moderate or large size is followed by a high mortality. Usually the patients requiring surgical operations are seen late in the course of the disease. The great majority of tumors requiring operation started as small papillomata of a low degree of malignancy which would have been readily amenable to treatment by simple transurethral procedures. The number of cases of papillomata, potentially malignant, but successfully treated by a skillful urologist as a routine office procedure is far greater than the number requiring extensive surgical operations. Certainly many cases are treated in the early stages with excellent results. The important thing is to find more of these cases, or all of them, while they are amenable to the simpler methods of treatment; when this occurs extensive surgical procedures will rarely be necessary.

The method of treating bladder tumors has changed rapidly in the last two decades and at present it varies considerably in different clinics. Exponents of certain methods of treatment such as x-ray and radium therapy and cystectomy have reported improved results in the treatment of their cases and thus influenced the general trend of treatment for a period of time. There is no single procedure that is suitable for all cases. *The best results have been obtained by operators with experience and judgment who are able to select the best treatment or combination of procedures for each individual case.*

The following methods of treatment of bladder tumors are most commonly employed at the present time.

1. *Transurethral procedures.* Transurethral procedures such as fulguration implantation of radium emanation seeds and removal of the tumor with the resectoscope should be done only in those areas that are readily accessible through the cystoscope. Papillomas up to 2 cm. in size can usually be controlled by simple fulguration. Larger tumors are generally considered malignant; nevertheless many, if they are not too large, respond to fulguration. If the tumor does not respond to three or four fulgurations, some other method of treatment is desirable.

For tumors too large to respond to fulguration transurethral resection when used by operators skilled in the use of the resectoscope gives good results especially with tumors of a low grade of malignancy. The removal of a solid tumor from a thin walled bladder with proper coagulation of the base is a delicate and risky procedure that calls for a high degree of technical skill. Recently many cases have been reported treated by this method with good results and low mortality. The tumor is resected sufficiently deep to expose the muscular layer of the bladder wall and this area then coagulated. Tumors weighing as much as 100 gm. have been removed in this manner. Following resection of tumors with a large base or those which have infiltrated the bladder wall, radon seeds may be implanted in the coagulated area as a further aid toward preventing recurrence. It is only in exceptional cases that the use of the prostatic resectoscope by the average operator is indicated. Many urologists advise against its use, favoring open methods of treatment.

2. *Suprapubic treatment.* The type of open surgical treatment employed depends on the extent and location of the growth. About 40 per cent of tumors occur on the lateral walls and in the vault, areas suitable for the removal of a segment of the entire vesical wall through a suprapubic opening. The

best results are obtained with this method of treatment, often called segmental resection, and it should be carried out whenever possible. The tumor and the entire thickness of the bladder wall should be resected with a cutting current which aids in the control of hemorrhage and avoids the spread of tumor cells in the operative field. A margin of normal bladder wall 1 cm. or more in width around the periphery of the tumor should be included in the resection. If the growth is comparatively small, or of a low degree of malignancy, or if it is an area unsuitable for resection, it may be excised with a portion of the bladder wall. The base is then thoroughly coagulated with a diathermy electrode and radon seeds planted if further treatment seems necessary.

Electrocoagulation or diathermy is the method of choice in destroying the flat, fairly extensive papillary growth of a low degree of malignancy. Occasionally growths which are apparently so extensive as to be inoperable respond surprisingly to thorough coagulation. On this account coagulation should be carried out, if possible, in patients with tumors that are seemingly inoperable; in a number there will be regression of the tumor.

There is a small group of cases in which the tumor is still confined to the bladder but is so located or so extensive as to preclude any possibility of cure by the usual methods of treatment. Cystectomy has been done in a number of these cases and reports of results have been increasingly more favorable. The mortality is high and the survival rate low, although in a group of recently reported cases satisfactory results have been obtained. Cystectomy demands that the urinary stream be diverted, which is usually carried out as a preliminary procedure. The bladder is then resected at a second operation. In some cases both procedures have been carried out at the same operation.

3. *Irradiation therapy.* High voltage x-ray therapy should be reserved for use in inoperable cases, for palliation and the arrest of hemorrhage. It is best suited to cases with a high degree of malignancy, as radiosensitivity tends to increase in proportion to malignancy. In occasional isolated instances x-ray therapy produces startling regression of the tumor. In those cases where, for various reasons, other more dependable methods cannot be employed, it may be of benefit.

There is little evidence to show that malignant tumors of the bladder can be cured by high voltage irradiation. Most urologists believe that it should be used only for patients who have advanced tumors, or for old and debilitated patients. In any case in which operation is suitable, it should be done.

4. *Implantation of radon.* Radon seeds have a definite place in the treatment of tumors of a high grade of malignancy. These seeds may be used in association with irradiation but they are most frequently employed following electrocoagulation. In tumors where seeds have been planted preoperatively through the cystoscope the proliferative power of the tumor cells, as observed postoperatively, is markedly reduced and in some cases completely destroyed. In other areas, nests of apparently intact malignant cells may be found. What benefit might be obtained by preoperative treatment is nullified by the increased technical difficulty of later surgical removal. The edema, swelling and friability of the irradiated tissue make it difficult and at times almost impossible to resect and close the bladder wall. On this account preoperative radium treatment is now rarely used.

SUMMARY

Tumors of the bladder, when treated during the early period of symptoms, respond readily to treatment and results can be obtained which are comparable to those obtained following treatment of tumors occurring in other parts of the body.

Intermittent hematuria is the most frequent and outstanding symptom of bladder tumor. Its prompt and complete, temporary disappearance, together with the lack of pain and discomfort, gives the patient and often the physician a false sense of reassurance, inviting procrastination in examination and treatment. Unfortunately, bleeding may not recur until a regrettably long period of time has elapsed.

Hematuria is always serious; it should never be ignored without definitely determining its origin. This necessitates a cystoscopic examination. If this is done as a routine measure, it will be possible to reduce substantially the distressingly high mortality from tumor of the bladder.

Given an early case, the chance of cure for the patient with a bladder tumor is dependent in large part upon the skill, knowledge, and experience of the cystoscopist.

"Cysts and Tumors of the Jaws," by Eugene W. Demaree, M.D., Chapter XIIA of the California Cancer Commission Studies will appear in this section of the January number of CALIFORNIA MEDICINE.

Correction

The name of one of the authors of Chapter XXII of the California Cancer Commission Studies, which appeared in the September issue of CALIFORNIA MEDICINE, was misspelled. The chapter, titled Carcinoma of the Liver, Gallbladder, Extrahepatic Ducts, and Pancreas, was written by William F. Roe, M.D., of Van Nuys, and E. Eric Larson, M.D., of Los Angeles. Dr. Roe's name was misspelled "Rowe."

Cancer of the Prostate

ROGER W. BARNES, M.D., *Los Angeles*

EVERY man who presents himself for physical examination should receive the benefit of digital palpation of the prostate through the anterior rectal wall. Routine investigation by this method familiarizes the examiner with the consistency, size, contour and sensitiveness of the normal gland, thus enabling him more readily to distinguish pathological changes, the most important of which is early malignancy.

Cancer of the prostate is found in 15 to 20 per cent of patients who have urinary obstruction due to prostatic enlargement. Some investigators have reported that 20 per cent of all men over 50 years of age have cancer tissue in the prostate gland but the majority of these die of other diseases before prostatic difficulties develop.

The pathological process usually originates in the dorsal portion of the prostate, near the capsule at its apex (the so-called posterior lobe), and may invade the entire gland from this point. It may, however, begin at any place in the gland. Sometimes islands of malignant tissue are found surrounded by benign hyperplasia, or the dorsal portion near the capsule may be malignant and the remainder of the gland benign. Cancer extends beyond the prostatic capsule early in the disease. Therefore, by the time a definite diagnosis can be made the lesion in most cases has extended too far for cure to be effected by radical prostatectomy. Later in the course of the disease, the neoplasm extends upward under the trigone, involving the seminal vesicles and encroaching upon the bladder neck, causing urinary obstruction.

The degree of malignancy of the neoplastic tissue determines the gross consistency of the gland and influences the prognosis. Most prostatic carcinomas are grade II (based on a four-grade classification), and are very hard and fixed. A few are grade IV, and these so resemble benign hyperplasia on rectal palpation that often the correct diagnosis of malignancy is not made preoperatively. When the process is highly malignant there is a shorter life expectancy.

Metastases to bone are of frequent occurrence late in the disease and are most commonly found in the pelvis. Usually they are osteogenic (increased calcium deposit); however, if the malignancy is high grade the bone lesion is osteolytic (decreased calcium deposit).

SYMPTOMS

The symptoms produced by carcinoma of the prostate are seldom manifested in the early stages of the disease. They are of two kinds; (1) obstructive, due to growth of the tumor into the prostatic urethra and bladder neck; and (2) pain, due to local extension or metastasis to bone.

Obstructive symptoms are usually first noticed by the patient, although occasionally a far advanced malignancy may be found without bladder disturbance. Urinary frequency, burning, slowness of the urinary stream, and irritation at the bladder neck are the presenting symptoms when the vesical outlet is encroached upon by the prostatic tumor. These may occur relatively early in the course of the disease if the cancer is associated with hyperplasia of the gland; in such cases symptoms are due chiefly to the benign lesion. When the obstruction is caused solely by the cancer, it occurs in the more advanced stage of the disease. Urinary tract infection, determined by the finding of pus and mixed microorganisms in the urine, usually develops when obstruction and residual urine have existed for a time. If this condition is allowed to persist for several years, dilatation of the upper urinary tract and impairment of renal function result.

Symptoms due to extension of the malignancy do not occur until the disease is advanced. Perineal or rectal pains or consciousness of this area may be the first symptoms. Low backache, pain in the groins, external genitalia, perineum and thighs, and later edema of the lower extremities are characteristic and may be very severe and constant. General malaise, weakness, loss of weight, and enlarged inguinal lymph nodes occur in the later stages of the disease, but are not usually present until the malignancy is widespread. Occasionally bone metastases occur beyond the pelvis and spine; when this takes place pain appears in the areas involved. Blood in the urine is never an early symptom or finding. It does not occur until the neoplasm has extended through the bladder or prostatic urethral mucosa, and even then it is not a constant finding. In fact, this symptom is much more common in benign hypertrophy than in carcinoma of the prostate.

DIAGNOSIS

If carcinoma of the prostate is to be cured by radical surgical operation, it is necessary that complete extirpation be accomplished before the neoplasm has extended through the perineural sheaths beyond the capsule. Because extension occurs early, the correct diagnosis must be made before the disease is advanced in order that it may be eradicated by operative removal. A presumptive diagnosis of carcinoma of the prostate in most cases can be made by digital palpation of the gland through the anterior rectal wall. *Inasmuch as the neoplasm most commonly originates in the dorsal portion of the prostate near the capsule, a hard, fixed nodule felt in this area is suggestive of malignancy.* The great difficulty in arriving at a diagnosis in early cases is that on palpation a localized area of inflammatory induration is often indistinguishable from a malignant nodule. It is impossible to make a positive early diagnosis by rectal palpation alone; careful histopathological study of the suspected area is the only means of establishing the diagnosis at this stage.

In order to obtain a satisfactory specimen for histopathological examination, the capsule of the prostate must be exposed through a perineal incision, the nodule identified and removed and a rapid frozen section made. If the tissue is found to be neoplastic, a radical perineal prostatectomy is done; if it is inflammatory the wound is closed without removal of the prostate unless there is obstruction due to benign hypertrophy. Opinion among urologists differs as to the advisability of this procedure. Some believe that every patient in whom a suspicious nodule is palpated should have immediate perineal exploration. Others maintain that this procedure is too radical because in a large proportion of cases microscopic examination discloses inflammatory induration rather than malignancy, and also that total perineal prostatectomy does not cure the disease in enough patients to be worth the risk entailed. It is wise for the physician to share the responsibility of making a decision in these cases by explaining the facts to the patient and by obtaining an opinion from a competent urologist.

Aspiration biopsy by needling the suspected area through the perineum and attempting to withdraw tissue cells for microscopic study is unreliable and is almost never indicated. Procurement of a specimen by endoscopic prostatic resection is not indicated unless bladder neck obstruction is present and the operation is directed primarily toward relief of the obstruction.

Carcinoma of the prostate is easily diagnosed in most cases in which the disease has progressed beyond the early stage. The characteristic stony hard and fixed gland as palpated by rectum is almost diagnostic; when the gland is irregular, nodular and enlarged the evidence is still more conclusive.

There are two conditions which must be differentiated from carcinoma: (1) Subacute prostatitis, which may present the same palpable characteristics as malignancy, especially when there is inflammatory induration of the periprostatic tissues. The onset of symptoms, however, is usually more acute, there is greater frequency and burning on urination, and a low grade fever is nearly always encountered. (2) Prostatic calculi, which are stony hard to rectal palpation, whereas the prostate as a whole is more movable and some elasticity is noticeable over the hard mass of calculi.

The prostate may contain malignant tissue yet not be hard and fixed on rectal palpation (1) when malignancy is high grade, as explained later in this chapter, in the section on "Pathology," and (2) when there is an island of neoplastic tissue surrounded by benign hyperplasia. Both these situations are comparatively rare.

Residual urine is found when there is bladder neck invasion by the neoplasm and when associated benign prostatic hypertrophy is sufficient to obstruct urinary outflow.

Cystoscopic examination is of some value in diagnosing prostatic malignancy in advanced cases but does not aid in the identification of early ones. When the prostatic urethra and bladder neck are invaded by the neoplastic process, rigidity of the vesical orifice is present, and nodules with prominent blood vessels in the mucosa which encroach into the urethral lumen, bladder neck and trigone (if the latter has been invaded) can be seen through the cystoscope.

Bone metastases are nearly always easily diagnosed by roentgenograms. However, metastatic deposits in bones or tissues may produce pain without being evident on x-ray films. Mottled areas of increased ossification (osteogenic) are seen in the roentgenogram of the pelvic bones. Sometimes the changes extend to the spine and ribs, and occasionally all the bones of the body are involved. If the prostatic malignancy is high grade, these bone changes may consist of areas of rarefaction (osteolytic). A comparatively new method of testing for metastases to the bones from carcinoma of the prostate is that of determining the acid-phosphatase content of the blood. When this is more than 4 mg. per 100 cc. it suggests such extension; if it is above 10 mg. it is practically diagnostic. Carcinoma of the prostate without bone metastases almost never produces an elevation in serum acid phosphatase. Alkaline phosphatase may be elevated with soft-tissue extension.

TREATMENT

Since the advent of endocrine therapy for carcinoma of the prostate, the outlook for patients who suffer from this disease is much brighter than formerly. There are five different courses of action which urologists now follow:

a. Immediate castration plus large doses of estrogens.

b. Estrogens alone as long as symptoms are controlled and there is no evidence of extension of the disease. Castration is thus reserved until the beneficial effect of the estrogen is lost.

c. Immediate castration, with administration of estrogen withheld until the disease extends.

d. Castration after extension of growth or metastasis is manifested, with estrogen prescribed later to neutralize androgens produced by adrenals.

e. Reduction of androgen production by exposure of the testicles to x-ray. This is used by only a few urologists and is probably not as effective as the administration of estrogens or surgical castration.

The most common and convenient method of administering estrogens is to give stilbestrol by mouth. The recommended initial dose is from 5 to 10 mg. per day, usually 2 mg. three times daily. If this medication causes nausea or gastric distress, enteric coated tablets can be given. These may not be effective if the coating does not dissolve and the tablets pass through the bowel without absorption. When excessive soreness of the nipples develops the dose is reduced to tolerance. It is continued indefinitely in maintenance doses of from 2 mg. a day to 2 mg. a week, usually about 1 mg. daily. When the patient cannot tolerate medication by

mouth, some other estrogen, such as estradiol dipropionate, 10 mg. daily as an initial dose, is given hypodermically.

When orchiectomy is performed, it is advisable to leave the epididymis on each side for esthetic reasons; the patient does not feel so emasculated if part of the scrotal contents is allowed to remain, even a small part. Sometimes the testicular tissue is removed and the entire tunica of the testes as well as the epididymes is left. Other urologists prefer the simplest and quickest procedure. From a medicolegal standpoint, it is not wise to perform castration unless the diagnosis of malignancy has been confirmed by histopathological study or by x-ray findings of bone metastases and elevated serum acid phosphatase.

Ten to 20 per cent of patients do not respond to endocrine therapy. However, in those who are susceptible to this treatment, the immediate results are almost miraculous. Within a week following the beginning of treatment the patient's pain has subsided and his appetite has returned; within two weeks he begins to gain weight and strength, and soon thereafter the enlargement and hardness in the prostate as palpated by rectum begin to melt away and urinary obstructive symptoms abate. If bone metastases have been demonstrated by x-ray these may disappear in a few months and in many cases every sign and symptom of the disease disappears. The unfortunate feature is that these changes represent only a temporary regression of the disease, not a cure. In some patients symptoms begin to reappear within a year; in others apparent absence of the disease may last eight or ten years.

For the group of patients who do not respond to estrogenic therapy, and for those who have recurrence of symptoms regardless of continued treatment, deep x-ray therapy is sometimes useful to relieve pain and to retard the malignant process. The administration of analgesics and other palliative measures are used to relieve pain. Permanent suprapubic cystostomy, indwelling urethral catheter, or frequent catheterization is necessary if urinary obstruction persists.

Radical perineal prostatectomy for removal of early prostatic malignancy has been discussed in the paragraph on diagnosis. In late cases the surgical treatment of this disease is concerned chiefly with the relief of vesical neck obstruction. Before transurethral prostatic resection was a common procedure, the most usual method of relieving obstructive symptoms was to perform suprapubic cystostomy for permanent bladder drainage. This is still the method of choice in patients in whom obstruction recurs within a few months after relief by transurethral resection and in those on whom this operation cannot be done because of urethral stricture or other reason.

Many patients who present urinary obstruction due to prostatic carcinoma will be relieved of this symptom only after several weeks of endocrine therapy. It is, therefore, wise to continue this treatment for a month or more before performing an operation to relieve the urinary retention. When there is a definite associated benign hypertrophy, obstructive symptoms will nearly always persist until relieved by operation. The transurethral approach is the method of choice because carcinoma of the prostate is very difficult to enucleate either suprapubically or perineally and a cure by any type of surgical intervention is rare except in very early cases. When there are islands of malignant tissue surrounded by benign hypertrophy, transurethral resection, if carried out completely and thoroughly, will cure as effectively as enucleation; however, the latter procedure is preferable to incomplete resection. Recurrence of vesical neck obstruction is common and when this occurs repeat transurethral resection of the bladder neck is necessary. Some authorities believe that 500 to 1,000 milligram hours of radium applied locally to the prostate will retard or prevent local growth. In some cases keeping the bladder neck dilated with sounds or a Kollmann dilator at frequent intervals may obviate the necessity for repeating the endoscopic operation.

Prostatic massage is not indicated in carcinoma of the prostate, and in fact may do considerable harm by disseminating neoplastic cells. It should be avoided whenever there is a probability of this disease.

PROGNOSIS

Carcinoma of the prostate is a slow-growing malignancy in most cases and the patient may live for as long as 15 or 20 years without treatment. The grade of malignancy has a definite bearing on the prognosis. The average length of life of the patient with a grade II tumor, which is the type most commonly found, is about four or five years when treatment consists of relief of urinary obstruction alone. The man who has a grade III or IV neoplasm has a life expectancy of only one to two years after onset of symptoms. Endocrine therapy has improved this prognosis considerably, but no definite statistics are yet available. It is probable that from two to five years will be added to the life expectancy of patients who respond to this treatment.

SUMMARY

1. Digital examination of the prostate through the anterior rectal wall should be included in the examination of every male patient. The presence of one or more small hard nodules is suggestive of early malignancy and a hard fixed gland is characteristic of further advanced carcinoma.

2. Symptoms may be due to obstruction to urinary outflow or to extension or metastases causing pain.

3. The administration of estrogens or the elimination of androgens by castration, or both, results in a remission of from one to six years in 80 to 90 per cent of cases. Transurethral prostatic resection is performed to relieve urinary obstruction, and radical perineal prostatectomy may be indicated in early cases. Prostatic massage is harmful.

California MEDICINE

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For Information on Preparation of Manuscript, See Advertising Page 2

EDITORIALS

The Heat's On

President Truman proved on November second that a one-man campaign, carried out in the face of apparently insuperable odds and against the glum predictions of his own followers, can be made to succeed. The nation has been stunned by the measure of success he achieved; it has admired his fighting methods even though it has had some cause to question his promises of all things to all people.

Among the promises was one to extend the provisions of the Social Security Act, an extension which has been painted and framed by his advisors and appointees in several departments of the Government. It includes, among other things, the extension of social security laws to employees not now covered by the law, the inclusion in the program of self-employed individuals (you, too, doctor), the increase of taxes against employer and employee and, certainly not least, the enactment of a national system of compulsory health insurance.

California doctors have long studied and opposed the establishment of a compulsory health insurance plan, either national or state. Now they are faced with a Democrat president and a Republican governor, both announced proponents of such a plan. If the doctors are to continue opposing a politically-operated system of medical practice, they must aim their weapons at both Washington and Sacramento.

There is no doubt that medicine has a fight on its hands. The chips are down and from now on it's a case of winner take all. Fortunately, the doctors have always won this fight and have as an advantage a string of victories and the accumulated knowledge of how they have been won. They know that other groups and organizations must be alerted to their own fate if the process of socialization is started against the medical profession. They know that the public must be advised of what is in store for Mr. and Mrs. John Q. when the heavy hand of bureaucracy takes over for bedside manners. They know that the public, once advised, will rise up in its own right and deny the right of politicians to take over for free choice of a physician who will render scientific care. They know that legislators must be particularly well advised on the implications behind this sort of vote-making machinery. Experience has taught the doctors these and many other things about socialized medicine, just as experience has taught them the bulk of what they know on the scientific side of medicine. There is room for improvement of techniques, certainly, but the old and time-tried measures will certainly form the basis for the development and application of the tactics needed now.

Some physicians have taken on a defeatist attitude since the election returns were counted. Some seem to think that, faced by both a national and a state threat, private medical practice is doomed. Some have advanced the theory that medicine had better go along with the tide and try to divert it into useful channels. Some are saying they are glad to be in their later years and on the road to retirement before the oncoming wave engulfs their sons and students.

To such as those mentioned above, perhaps Mr. Truman has served up a good example. Perhaps he has, by his own actions, proved that a good fight can always be made when you believe you have the right on your side and maintain confidence in the public. Perhaps his vigorous campaign against heavy odds has lighted the path along which medicine, as a supposed underdog, can travel to victory.

The heat's on. Let's roll up our sleeves and go to work.

Hats Off

Medical practice on the distaff side has come a long way from its former position of being tolerated if not just plain ignored by the male members of the profession. Where once the woman physician was a rarity, today we are accustomed to seeing more and more practitioners in skirts, many of them definitely in fields such as industrial medicine where doctors in trousers are usually exclusively in attendance. The gentler aspects of laboratory work and obstetrics can no longer lay sole claim to the services of our female confreres.

The ladies have advanced in another direction, too. They have entered wholeheartedly into the economic and political sides of medical practice and have proved their right to be heard and respected in these fields. Their counsel has been invaluable on many occasions.

All of which brings us to a salute to Dr. Leslie S. Kent of Eugene, Oregon, first woman physician to be honored by her fellows by election to the presidency of a state medical association. Doctor Kent has labored long in an active medical practice and in organization affairs. She took a leading part in medical dealings with the warborn EMIC program and has become well and favorably known in many medical organizations outside her own state. Her election to high office in Oregon bears out the confidence which her many friends have in her and the respect in which she is held.

Congratulations to Doctor Kent and to the Oregon State Medical Society which elected her president. Hats off to the ladies and, particularly, to our good friend Leslie Kent.

Woman Also Works

Periodically the California State Division of Industrial Welfare finds it necessary to call attention to the laws regarding the employment of women in industrial, general, business or professional offices. That time has come again and the state agency has come up with a gentle reminder that women and minors are, in the eyes of the law, a little different from men employees.

For instance, a woman employee may not be scheduled to work more than eight hours in any one day. In case of emergency she may work more than eight hours but the overtime must be paid for at one and one-half times the regular wage rate. She must be paid a minimum wage of 65 cents an hour (if you can find anyone at that rate) and must be given a regular rest period, say ten minutes, morning and afternoon. She must be allowed a meal period of not less than 30 minutes not later than five hours after she reports for work. Her starting and leaving time must be recorded, along with the number of hours worked and total wages received in each payroll period.

Some of these requirements will appear elementary to many physicians but in those rare instances where they are not lived up to, the employing doctor may run afoul of the law. To be safe, instead of sorry, write the Division of Industrial Welfare at 404 State Building, Los Angeles 4, or 865 Mission St., San Francisco 3, for a copy of Order No. 4R, which tells all about it.

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NOTICES AND REPORTS

Council Meeting Minutes

Tentative Draft: Minutes of the 356th Meeting of the California Medical Association, Los Angeles, October 30-31, 1948.

The meeting was called to order by Chairman E. L. Bruck in Conference Room 5 of the Biltmore Hotel, Los Angeles, at 9:30 a.m., Saturday, October 30, 1948.

Roll Call:

Present were President Askey, President-Elect Kneeshaw, Council Chairman Bruck, Speaker Alesen, Vice-Speaker Charnock, Councilors Crane, Henderson, Anderson, Ray, Lum, Pollock, Green, Cherry, MacLean, Hoffman, Bailey and Thompson, and Editor Wilbur.

Absent: Councilor Ball. Excused: Councilor Shipman and Secretary Garland.

Present by invitation were Dr. Dwight H. Murray, chairman of Public Policy and Legislation; Executive Secretary John Hunton; Assistant Executive Secretary William P. Wheeler; Legal Counsel Howard Hassard; Mr. Ben H. Read, executive secretary of the Public Health League of California; Mr. Ed Clancy, field secretary; Mr. James J. Boyle, Washington representative of the United Public Health League; Doctors Malcolm Merrill and Edward Kupka of the California State Department of Public Health; Doctor William Gardinier and Mr. John McMahon of California Physicians' Service, and county society executive secretaries Rollen Waterson of Alameda and Stanley K. Cochems of Los Angeles.

A quorum present and acting.

1. *Minutes:*

(a) On motion duly made and seconded, minutes of the 355th meeting of the Council, held August 21-22, 1948, were approved.

(b) On motion duly made and seconded, minutes of the 211th meeting of the Executive Committee, held August 22, 1948, were approved.

(3) On motion duly made and seconded, minutes of the 212th meeting of the Executive Committee, held September 29, 1948, were approved.

Special Recognition for 50-Year Members

Seven members of the California Medical Association have been reported by the secretaries of their county societies as eligible for the special recognition which the Council voted shall be given to those who have maintained membership in the association for 50 years or more.

Just what the token of recognition is to be has not yet been decided by the Council, but wall plaques and lapel emblems have been considered.

The seven members on the present list of eligibles are:

G. W. Duffing, Sacramento County
Andrew Henderson, Sr., Sacramento County
Herbert C. Moffitt, San Francisco County
James Seymour, San Francisco County
William Stephens, San Francisco County
W. I. Terry, San Francisco County, and
G. W. Sevenman, San Mateo County.

Eligibility is established through the records of the component county societies of the C.M.A. Any member who believes himself eligible but is not one of the seven named above is requested to call the matter to the attention of the secretary of the county society of which he is a member.

2. *Membership:*

(a) A report of membership as of October 28, 1948, showing 9,180 active and associate members, was received and ordered filed.

(b) On motion duly made and seconded, one member whose 1947 dues had been received since August 22, 1948, was voted reinstatement.

(c) On motion duly made and seconded, twenty-four members whose 1948 dues had been received since August 22, 1948, were voted reinstatement.

(d) On motion duly made and seconded, rules and regulations covering the reduction of dues for members who are absent from their practices for extended periods because of illness or postgraduate study, prepared by a special Council committee, were approved.

(e) On motion duly made and seconded, a reduction of dues was granted to seven members who were recommended for such reduction by their county societies because of illness or postgraduate study. These were:

Dean S. Scofield, Los Angeles County.
Erwin P. Brauner, Orange County.
Fred E. Abbott, San Diego County.
William M. Wilson, Jr., San Diego County.
Isabella H. Perry, San Francisco County.
W. E. Jensen, Santa Cruz County.
Thomas F. Keyes, Yuba-Sutter-Colusa County.

(f) On motion duly made and seconded, thirty applicants for affiliate membership were voted such membership on nominations by their county societies.

(g) Seven members who had been reported by their county societies as having maintained membership for fifty years or more were, on motion duly made and seconded, elected to receive an emblem honoring their long term as active members. A suitable emblem was selected and it was agreed to make the presentation at each Annual Session. The members so elected were:

G. W. Duffing, Sacramento County.
Andrew Henderson, Sr., Sacramento County.
Herbert C. Moffitt, San Francisco County.
James Seymour, San Francisco County.
William Stephens, San Francisco County.
W. I. Terry, San Francisco County.
G. W. Sevenman, San Mateo County.

3. *Financial:*

(a) A report of bank balances as of October 28, 1948, was received and ordered filed.

(b) Report was made that $130,000 in current funds had been invested in U. S. Treasury bills, which mature in 90 or 91 days, and that $25,000 in funds held by the Trustees of the C.M.A. had been invested in U. S. Treasury 2½ per cent bonds, due 1972.

4. *Memorial to P. K. Gilman, M.D.:*

The Council discussed the establishment of a memorial to the late Philip Kingsnorth Gilman, M.D., former Councilor and former President of the Association. On motion duly made and seconded, it was voted to establish a $1,000 memorial fund at Stanford University School of Medicine. It was agreed that this fund should, if possible, carry Doctor Gilman's name. Dr. Dwight Wilbur was instructed to continue his efforts to determine the most effective application of the fund.

5. *California State Department of Public Health:*

Dr. Malcolm Merrill of the California State Department of Public Health displayed charts and figures on the polio situation, pointing out that the number of cases reported in 1948 was approaching the 1934 record high and would probably pass the 1934 figure. Peak of the cases came in September, which is later than usual, and the trend is now downward.

Doctor Merrill also discussed several items which will account for the bulk of the increase in budget which the Department is seeking for the 1949-1950 fiscal year. Major items in the increase will be (1) additional sanitary engineers to handle the sewage, water and other problems aggravated by a greatly increased population; (2) establishment of schools of physiotherapy for cerebropalsy cases; (3) establishment of a pattern for state aid to the counties for crippled children's cases; and (4) increased studies of Q fever, following the withdrawal of most U. S. Public Health Service personnel at the end of 1948.

Doctor Merrill reported that the State Department of Public Health's tuberculosis control program would be well served by a committee composed of representatives of the Department, of the California Medical Association and of the California Tuberculosis and Health Association. On motion duly made and seconded, it was voted to name a representative of the Association to such a committee. The Chairman appointed Dr. H. Gordon MacLean to this position.

Doctor Merrill discussed the proposed mass mini-film x-ray survey for tuberculosis. Survey teams would be sent into California by the U. S. Public Health Service in 15 to 18 months, to make films of all people above 16 years of age in the metropolitan centers. Estimates show 6,000,000 people in these four areas, and an estimated 4,000,000 films would be made; of this number, an estimated 3½ per cent would show some chest pathology and about one case of tuberculosis per 1,000 films would be expected, about 90 to 95 per cent of this number being previously unknown. Cost would run about $500 for each active case uncovered. Active cases of tuberculosis or other chest conditions would be referred to private family physicians. Approval of the State Department of Health and of the California Medical Association would be required before the U.S.P.H.S. would undertake the survey.

On motion duly made and seconded, it was voted to defer action on this request pending further study, including the determination of the attitude of medical associations in areas where similar surveys have already been made.

Doctor Bruck reported that the Chronic Disease Study advisory committee had met and that proposed portions of the report of the advisory committee had been drafted. These will go to an editing committee which will put them into final shape for presentation to the committee. Doctor Bruck read

the preliminary proposed reports covering research, state planning and administrative research, and diagnostic and therapeutic services. Suggestions were offered for amending the preliminary drafts and the amended reports approved.

Dr. Lyell C. Kinney, chairman of the Cancer Commission, appeared before the Council and read the preliminary proposed report of the section on cancer for the same report. Amendments were offered and the amended report approved.

6. *Physicians' Benevolence Committee:*

Dr. Axcel E. Anderson, chairman of the Physicians' Benevolence Committee, requested nominations for appointment of a member to the committee, to succeed Dr. Robert A. Peers, retired. On motion duly made and seconded, it was voted to extend this appointment to Dr. John W. Sherrick of Oakland.

7. *Advisory Planning Committee:*

Mr. Hunton reported that the Advisory Planning Committee had held two meetings and had taken two actions on which Council approval was requested. (1) It was decided to make transcriptions of a radio series entitled "If They Had Lived Today," produced by Mr. Stanley Cochems of Los Angeles, and make these transcriptions available to other county medical societies which wished to use them. The Council approved this action as a part of the public relations program. (2) The Committee recommended that copies of the Brookings Institution study on compulsory health insurance be purchased and sent to all public school libraries in California. Copies would cost $1.50 each and about 2,000 copies required. On motion duly made and seconded, the Council voted to approve this program and expenditure.

8. *Committee on Scientific Work:*

A resolution clarifying Council instructions to the Committee on Scientific Work regarding the number of C.M.A. guest speakers invited to Annual Sessions was presented. Five guest speakers are now authorized. Sections sometimes wish to invite outstanding speakers in their own fields, expenses of such being borne by members of the section or specialty group; in some instances such guests might be regarded as official guests of the Association itself. On motion duly made and seconded, it was voted that guest speakers beyond the authorized five each year, may be invited by specialty sections, the question of whether such guests are to be considered as guests of the Association to be decided by the Committee on Scientific Work.

9. *California Physicians' Service:*

Mr. John McMahon, assistant director of C.P.S., reported that as of October 1, 1948, membership in C.P.S. totaled 615,444 in the commercial program. September enrollment was 25,060, of which 40 per cent was new membership groups and 60 per cent additions to existing groups. Individual enrollment is being tried out in Eureka and experience to date shows that individuals will not respond to newspaper advertising or radio appeals but must be individually solicited.

Dr. William Gardinier, assistant medical director, reported that physician membership as of October 1, 1948, was 9,178. The financial report as of September 1, 1948, showed $416,000 in the unit stabilization fund reserve and showed that $5,000,000 had been paid to physicians for their services in the first five months of the present fiscal year.

There was discussion relative to C.P.S. and it was regularly moved, seconded and voted to include in the next Council meeting a joint session with the trustees of C.P.S.

10. *Blue Shield-Blue Cross Proposals:*

Mr. Hassard discussed the recent meeting in French Lick Springs, Indiana, of the Blue Shield and Blue Cross plans, at which a proposed establishment of a national enrollment agency was under consideration. The conference resulted in three decisions: (1) That a national organization be discussed but not acted upon at that meeting. (2) That Blue Shield member plans discuss the national organization proposal with their own sponsoring state or county medical association, and (3) that the proposal be referred to the A.M.A. House of Delegates by a committee appointed to make such presentation in conjunction with the A.M.A. Council on Medical Service.

The American Hospital Association has approved the proposed national organization, in which the Blue Cross Commission of the A.H.A. would participate. The Blue Cross plans voted at the recent French Lick meeting not to go ahead on plans of their own for establishment of a national program offering hospitalization and medical-surgical indemnity until the A.M.A. House of Delegates has had a chance to consider the proposed joint program; in the event the A.M.A. votes against the proposed plan, the Blue Cross plans have indicated their intention to establish their own national enrollment program but in this case have agreed to leave the way open for Blue Shield plans to participate if a later decision makes this possible.

On motion duly made and seconded, it was voted to recommend to the California Delegates to the American Medical Association that they vote against the proposed national enrollment organization plans unless the medical phases of such plans are placed directly under the control of the A.M.A.

11. *Emergency Medical Service:*

On motion duly made and seconded, it was voted to appoint a committee of five as a Committee on Emergency Medical Service, to cooperate with the Committee on National Emergency Medical Service of the American Medical Association. The Chairman, authorized to make such appointments, appointed Drs. L. A. Alesen of Los Angeles, chairman; Carleton Mathewson, San Francisco; Lewis T. Bullock, Los Angeles; Frank A. MacDonald, Sacramento; and Orris R. Myers, Eureka.

12. *Blood Banks:*

The Chairman read a progress report from Dr. John Upton, chairman of the Blood Bank Commission, and the report was received and ordered filed.

13. *California Medicine:*

Dr. Dwight L. Wilbur, editor of CALIFORNIA MEDICINE, reported that a proposed publication of annual medical reviews by a Chicago physician and his associates did not appear feasible for inclusion as a supplement to CALIFORNIA MEDICINE and that he had suggested to the authors that paid advertising might be run to promote its sale. It was regularly moved, seconded and voted that this publication should be considered as a commercial venture, eligible for advertising in the journal.

Mr. Hunton, on behalf of the advertising committee, requested clarification of the Council attitude toward the acceptance of liquor advertising. It was regularly moved, seconded and voted that alcoholic beverage advertising be not accepted pending further action by the Council.

At this point, 1:45 p.m., the Council recessed until 9:30 the following day.

14. *Reconvention:*

The Council reconvened at 9:30 a.m., Sunday, October 31, 1948, in Conference Room 5 of the Biltmore Hotel, Los Angeles. A roll call showed all those present the preceding day to be present. A quorum present and acting.

15. *Association Mailing List:*

Doctor Alesen requested that the Association mailing list be made available to the Investors League, Inc., to aid that organization in its campaign against governmental encroachment on private enterprise in business or professional life. It was regularly moved, seconded and voted that the mailing list be made available to this organization and that public relations counsel be asked to give possible assistance in this move.

16. *Legal Department:*

Mr. Hassard reviewed a malpractice case in Lodi, in which new judicial interpretations of the law had emerged. He stated that his office, acting on Executive Committee authorization by telephone, had filed a brief as amicus curiae. The Council approved this step and authorized the moderate printing and filing costs involved.

Mr. Hassard also reviewed the opinion rendered by the Attorney General of California holding that a hospital may not engage in the practice of medicine through the employment of physicians on salary. A New York attorney for the American Hospital Association has rendered an opinion that *non-profit hospitals* may engage physicians on salary but the attorney for the Association of California Hospitals has advised his client that the Attorney General's opinion is sound and must be followed. A conference is scheduled for November 8, 1948, to discuss this matter and Mr. Hassard has been invited to attend.

17. *Public Policy and Legislation:*

Dr. Dwight H. Murray, chairman of the Committee on Public Policy and Legislation, distributed copies of a draft of a proposed bill to establish a "Practical Nurses Act" prepared by the California State Nurses Association. After discussion it was regularly moved, seconded and voted to appoint a committee to meet with nurse association representatives to discuss this proposal. The Chairman named Doctor Murray, Doctor MacLean and Mr. Hassard to this committee.

Doctor Murray also discussed a physical therapy bill which is expected to be introduced in the next Legislature, similar to previous bills of this nature which have consistently been defeated. Representatives of recognized physical therapy schools have requested Mr. Hassard to draft a suitable bill for their presentation in the Legislature, which he had agreed to do provided (1) the Council approve and (2) he would be solely entrusted with such draft and its progress in the Legislature. On motion duly made and seconded, Mr. Hassard was authorized to proceed on this basis.

Mr. Read gave a brief report on the California election campaign and Mr. Boyle reported on the national legislative outlook.

A resolution adopted by the Council of the San Diego County Medical Society, decrying the proposed establishment of Social Security laws to cover self-employed individuals and urging a stand against such legislation, was read and it was regularly moved, seconded and voted that the substance of the resolution be approved and the San Diego Council commended for its activity and interest in this matter.

Letters from two members, urging support for Marjorie Shearon, Ph.D., were read and it was regularly moved, seconded and voted to continue the Association's support of her service.

18. *Diabetes Survey:*

A letter from the Alameda County Medical Association, reporting on a proposed county-wide survey for diabetes, was read and it was regularly moved, seconded and voted to disapprove this project.

A second proposed diabetes survey, sponsored by the American Diabetes Society, was approved, with the provision that the survey be conducted through the appropriate county medical societies.

19. *Committee Report on Membership Qualifications*

A report by a special committee under the chairmanship of Dr. John W. Cline on a resolution introduced by Dr. Wilbur Bailey at the 354th Council meeting, was read and, with minor amendments, approved.

20. *California Ambulance Association:*

Doctor Hoffman reported on meetings with representatives of the California Ambulance Association, which is seeking medical advice in setting up a code of ambulance standards, and urged that cooperation of the Association be extended. Doctor Hoffman has been asked to sit as a non-voting member of the organization's executive board and to address its meeting in Fresno on November 21, 1948. The Council approved these requests.

21. *Crippled Children's Program:*

Attention was called to Resolution No. 23 adopted by the 1948 House of Delegates relative to an investigation into the authority of officials in administering the Crippled Children's Act and it was regularly moved, seconded and voted that a committee for this purpose be appointed. The Chairman appointed Drs. John C. Sharp and Lloyd Hardgrave.

22. *Sister Kenny Foundation:*

A request for Association cooperation in the administration of the program of the Sister Kenny Foundation was read. It was pointed out that the San Francisco County Medical Society has been studying a similar request and it was agreed to await word from that study before further Council consideration is given.

23. *Employees' Retirement Program:*

Doctor Charnock reported that a life insurance-retirement annuity policy has been issued to the Association on the life of John Hunton. The committee has not yet met to consider recommendations for extending this program to other employees who might become eligible.

24. *American Public Health Association:*

Attention was called to a meeting in Boston, November 8-12, of the Committee to Consider Establishment of a Medical Care Section of the American Public Health Association. It was regularly moved, seconded and voted to appoint a C.M.A. representative to attend this meeting, the Chairman to select the representative. Dr. William P. Lucas, a fellow of the A.P.H.A., was appointed.

25. *General Practitioner of 1948:*

Mr. Hunton reported that only one nomination had been received from county medical societies for nomination by the Association to the A.M.A. for consideration for the General Practitioner award for 1948. It was agreed to ask the Executive Committee to await further nominations and to make a selection for nomination at the latest available time.

26. *A.M.A. Grass Roots Conference:*

On motion duly made and seconded, Dr. Robertson Ward was elected as C.M.A. representative to the "Grass Roots" Conference of the A.M.A.

Veterans' Views on the Home Town Medical Care Program

A recent survey was initiated by California Physicians' Service, at no expense to the government, in order to determine the effectiveness of the Veterans Home Town Care Program. The veterans who have received treatment were asked to judge how successful the California Physicians' Service had been in rendering treatment. Comments were requested bearing on all phases of the program, particularly in contrast to other types of medical care which they, as veterans, have received in the past.

FAVORABLE COMMENTS

1. Free choice of physician provides personal care which is better than any other method	54%
2. Saves time and trouble while permitting self-employment and education	15%
3. Provides relief from congestion in VA hospitals with a minimum of "red tape"	10%
4. Ability to maintain home due to relief from financial burden	7%
5. Specific requests to continue program	6%
	92%

UNFAVORABLE COMMENTS

1. Delay in treatment 2. Delay in payment of bills 3. Red tape	8%

The unfavorable replies represent cases which require either a change in the law, further coordination within our own offices, or improved liaison with the Veterans Administration.

It is to be noted that the written replies received conform to the verbally expressed opinions of the hundreds of veterans who have called personally at our offices.

The final conclusion must be that this plan has filled a tremendous gap in completing the desire of the government to give the best and most adequate care to our disabled veterans, and that the plan, its administration, and its effectiveness, while not perfect, is preponderantly the best yet developed for ambulatory cases.

The success of the program has been made possible due to the excellent cooperation of the physicians, the veterans, the California Physicians' Service and the officials of the Veterans Administration in California whose daily assistance has been most important.

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27. *Insurance Payments to Chiropractors:*

A resolution from the Sacramento Society for Medical Improvement was read, objecting to plans of some insurance companies to provide payment for chiropractic services under accident and health insurance policies. It was regularly moved, seconded and voted to advise the Society that the Council agreed with the resolution and would take the matter up with the insurance companies.

28. *U. S. Public Health Service Tuberculosis Meeting:*

A request from the U. S. Public Health Service to use the Association's mailing list in arranging a San Francisco Bay Area meeting on tuberculosis problems was discussed and approved.

29. *Time and Place of Next Meeting:*

It was agreed that the next meeting of the Council should be held in San Francisco on December 18 and 19, 1948.

30. *California Farm Bureau Federation—Brucellosis Proposals:*

A report from Dr. Paul Michael of Oakland on a meeting of the California Farm Bureau Federation in connection with proposals for the control of brucellosis was read and approved. It was voted to commend Doctor Michael for his efforts in this matter and to suggest his continued interest.

Adjournment.

In Memoriam

BALLARD, SAMUEL EDWARD. Died in Long Beach, September 20, 1948, aged 74. Graduate of the Baltimore Medical College, Maryland, 1899. Licensed in California in 1916. Doctor Ballard was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

✤

BROWN, HENRY ALEXANDER. Died in Los Altos, September 19, 1948, aged 77, after an extended illness. Graduate of the Medico-Chirurgical College of Philadelphia, 1900. Licensed in California in 1917. Doctor Brown was a retired member of the Alameda County Medical Association, and the California Medical Association.

✤

CRUICE, LEMAN DOW. Died in Alhambra, September 27, 1948, aged 60, of a heart attack. Graduate of the Jefferson Medical College of Philadelphia, Pennsylvania, 1913. Licensed in California in 1931. Doctor Cruice was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

ENGSTROM, WALFRED A. Died in South Gate, October 23, 1948, aged 40, when he was struck by an automobile. Graduate of the College of Medical Evangelists, Loma Linda-Los Angeles, 1944. Licensed in California in 1944. Doctor Engstrom was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

✤

FARRAGE, JAMES. Died in Corona, October 5, 1948, aged 48, of a heart attack. Graduate of the University of Southern California School of Medicine, Los Angeles, 1934. Licensed in California in 1934. Doctor Farrage was a member of the Riverside County Medical Society, the California Medical Association, and the American Medical Association.

✤

HALLOCK, PHILLIP. Died in Los Angeles, June 29, 1948, aged 46. Graduate of the University of Minnesota Medical School, Minneapolis, 1929. Licensed in California in 1945. Doctor Hallock was a member of the Los Angeles County Medical Association, the California Medical Association, and the American Medical Association.

✤

HORNER, WARREN DOUGLAS. Died in San Francisco, October 22, 1948, aged 58, following an extended illness. Graduate of the University of California Medical School, Berkeley-San Francisco, 1916. Licensed in California in 1916. Doctor Horner was a member of the San Francisco County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

✤

JAMES, VOYLE MUSSER. Died in North Hollywood, October 17, 1948, aged 49, of a heart attack. Graduate of the New York University College of Medicine, New York, 1924. Licensed in California in 1927. Doctor James was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

JONES, LLEWELYN L. Died in Glendale, October 17, 1948, aged 77, when he was struck by an automobile. Graduate of the University of Nashville Medical Department, Tennessee, 1899. Licensed in California in 1921. Doctor Jones was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

JONES, ROBERT MELVIN, JR. Died in Bakersfield, October 17, 1948, aged 66, after a long illness. Graduate of Vanderbilt University School of Medicine, Nashville, Tennessee, 1913. Licensed in California in 1913. Doctor Jones was a member of the Kern County Medical Society, the California Medical Association, and the American Medical Association.

✤

LAIST, OTTO. Died in San Francisco, October 13, 1948, aged 77. Graduate of the College of Physicians and Surgeons of San Francisco, 1900. Licensed in California in 1900. Doctor Laist was a retired member of the San Francisco County Medical Society, and the California Medical Association.

✤

REED, EDWARD NORTH. Died in Sawtelle, October 19, 1948, aged 71. Graduate of Rush Medical College, Illinois, 1904. Licensed in California in 1914. Doctor Reed was a retired member of the Los Angeles County Medical Association, and the California Medical Association.

✤

SHERMAN, BENJAMIN HARRY. Died in Los Angeles, October 18, 1948, aged 69. Graduate of Northwestern University Medical School, Chicago, Illinois, 1904. Licensed in California in 1915. Doctor Sherman was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

✤

SPERRY, JOHN AUGUSTUS. Died in Burlingame, September 29, 1948, aged 66, of a heart attack. Graduate of Tulane University of Louisiana School of Medicine, New Orleans, 1905. Licensed in California in 1917. Doctor Sperry was a member of the San Francisco County Medical Society, the California Medical Association, and the American Medical Association.

✤

WILLIAMS, FORREST EARL. Died on a train west of Evansville, Wyoming, aged 53, of coronary thrombosis. Graduate of the Northwestern University Medical School, Chicago, Illinois, 1924. Licensed in California 1939. Doctor Williams was a member of the Monterey County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

NEWS and NOTES

NATIONAL • STATE • COUNTY

LOS ANGELES

Appointment of **Dr. Myron W. Husband** as district health officer for the Glendale district of the Los Angeles County Health Department has been announced by **Dr. Roy O. Gilbert**, county health officer. The appointment fills a vacancy created by the resignation of **Dr. Francis Hillman. Dr. Hiram Gallagher**, member of the staff who administered the office until Dr. Husband was appointed, will remain as assistant.

* * *

Dr. Paul Starr, member of the faculty of the graduate division of the University of Southern California School of Medicine, has been appointed professor of medicine and acting chairman of the department of medicine, according to announcement from the office of **Dr. Burrel O. Raulston**, dean of the medical school.

* * *

The first annual **mid-winter radiological conference** sponsored by the Los Angeles Radiological Society will be held in the Biltmore Hotel, Los Angeles, February 26 and 27, 1949. Courses will be given by prominent Pacific Coast radiologists, and on Saturday evening, February 26, **Dr. Frederick Templeton** of Seattle will speak on "The Differential Diagnosis of Benign and Malignant Gastric Lesions." Reservations can be made by writing Dr. Donald Laing, 65 N. Madison Avenue, Pasadena 1, California. The fee for the two-day session is $15.

MARIN

A pledge to cooperate with the California Medical Association **blood bank program** by transporting blood or plasma by plane if necessary in emergencies, such as might arise in connection with disaster, has been given by the Marin County sheriff's air patrol. Glenn Wentz, captain of the air patrol, said that this assistance had been asked in a letter from **Dr. John R. Upton**, chairman of the California Medical Association Blood Bank Commission which is endeavoring to set up a system for making adequate supplies of blood available for transfusions in all communities in the state.

SAN BERNARDINO-RIVERSIDE

Dr. C. T. Halburg of Redlands was elected president of the San Bernardino-Riverside counties chapter of the American Academy of General Practice at the final organizational meeting of the chapter. **Dr. Henry Barron** of Riverside was elected vice-president and **Dr. Norman E. Marsh**, San Bernardino, secretary-treasurer.

SAN DIEGO

A new psychology commission of five members has been appointed for the City of San Diego for the purpose of wiping out the menace of unqualified "psychologists" treating mental disorders. The commission, formation of which was ordered by the city council, will process all licenses of practicing psychologists. Psychologists now practicing and those wishing to enter practice will be required to make formal application for a license.

The members of the new commission are: Dr. Ivan McCollom, head of the psychology department at San Diego State College; Dr. Melvin W. Barnes, director of the University of California Extension Division for the San Diego Area; Dr. Jessie Marcia Ostrander, a clinical psychologist in private practice; Dr. Fay Perry, director of guidance at San Diego State College, and Dr. Thomas Law Coyle, minister of the First Presbyterian Church. Dr. McCollum, Dr. Barnes and Dr. Ostrander are members of the American Psychological Association. The ordinance establishing the commission requires that three of the five members be members of that association.

SAN FRANCISCO

An essay contest with two prizes, one of $150 and the other $100, has been announced by the **San Francisco Surgical Society**. It is open to physicians in the field of general surgery, residing within a 50-mile radius of San Francisco, who are in the period of graduate training and not more than six years removed from graduation from medical school. Full rules of the contest may be obtained from Dr. Leon Goldman, secretary of the society, University of California Hospital, San Francisco 22.

* * *

Dr. Monroe Jerome Hirsch has been appointed acting assistant professor of physiology at Stanford School of Medicine. He was formerly assistant professor of physiology at Ohio State University and before that a research associate at Stanford.

* * *

A **hearing center** to which persons with auditory impairment may be referred by physicians for extensive hearing tests and fitting of hearing aids has been established by the San Francisco Hearing Society with the guidance of a committee of otologists working under the San Francisco County Medical Society. Anyone with auditory impairment may avail himself of the services of the center, which is expected to be self-supporting from the fees charged private patients. Fees are on an established schedule but take into consideration the ability of the patient to pay. A recent otologic examination is required, and those not referred to the center by a physician will be given a list of qualified doctors, so that they may impartially select one for the required preliminary examination.

The center is equipped to administer complete pure tone and speech audiometric tests in a sound-treated room. Arrangements have been made with several local dealers of A.M.A.-approved hearing aids to obtain their latest models for demonstration purposes. It is contemplated that in the near future classes and individual instruction in auditory training, lip reading and speech will be available at the center. Eventually, psychological counseling and vocational guidance will be included.

SAN JOAQUIN

Dr. John O. Eccleston recently was appointed city physician of Stockton and director of the Emergency Hospital to take the place of **Dr. H. S. Chapman**, who resigned several months ago after 28 years' service.

SAN MATEO

Dr. H. L. Wynns has been appointed to the new post of superintendent of field services of the San Mateo County department of health by the county health and welfare advisory board. The new position supplants that of chief of communicable diseases which has been discontinued. Dr. Wynns formerly was assistant district health officer in San Joaquin County, where he served with Dr. Harold D. Chope who is now San Mateo County health director.

SANTA CLARA

The Santa Clara County Mental Health Service, which will be available to adults for advice and consultation on personal matters relative to mental health, has been established with funds allotted by the California Department of Public Health and soon will be in operation. President of the service is Dr. Dwight M. Bissell, who is also president of the Mental Hygiene Society of Santa Clara County, the organization which has been working for establishment of the service. Dr. Rush Faville of Palo Alto will be chief of service.

Directors of the organization said Santa Clara County is one of the few in California having a mental health service of this kind for adults, although recently in San Mateo County a child guidance clinic was established with Dr. Paul Holmer as director.

SOLANO

Establishment of a new county hospital at Vallejo was advocated by a number of Vallejo physicians attending a recent joint meeting of the Solano County Medical Society and the local unit of the Tuberculosis Association which had been called to discuss plans for a hospital for tuberculous patients and expansion of existing county hospital facilities. Pointing out that hospital facilities in Vallejo are inadequate, the Vallejo speakers urged that the county erect a new structure in the area's greatest center of population. It was suggested that the present hospital at Fairfield might then be used as a home for aged indigents.

TULARE

Dr. E. G. Johnson has resigned as assistant director of the Tulare County Hospital to enter private practice but will continue to make visits to the hospital when necessary until the board of supervisors is able to obtain a physician to fill the vacated post.

GENERAL

Of 100 full-time positions open to physicians in tuberculosis hospitals of the Veterans Administration, six are in California, Arizona and Nevada, according to an announcement by the government agency. Salary scale for the posts now open ranges from $4,479 to $10,305. Applicants are asked to address inquiries to Veterans Administration Branch Office 12, 180 New Montgomery St., San Francisco 5, or to Chief Medical Director, Veterans Administration, Washington 25, D. C.

Dr. Donald G. Tollefson, associate clinical professor of obstetrics and gynecology, University of Southern California Medical School, was elected first vice-president of the American College of Surgeons at the annual meeting in Los Angeles, October 21. Dr. Gilbert J. Thomas of Beverly Hills was reelected to the board of regents for a term expiring in 1951. Elected to the board of governors were Dr. H. Glenn Bell and Dr. Emile Holman, both of San Francisco; Dr. Clarence J. Berne and Dr. E. Eric Larson of Los Angeles, and Dr. Clarence E. Rees, San Diego.

* * *

The Phi Delta Epsilon Northern Fraternity, of which some 600 physicians in California are members, will hold its national convention in San Francisco, December 26, at the Fairmont Hotel.

* * *

Dr. William F. Quinn of Los Angeles was elected president of the California State Board of Medical Examiners at a recent meeting, succeeding Dr. Richard O. Bullis, also of Los Angeles. Dr. Clayton D. Mote of San Francisco was elected vice-president of the board, and Dr. Frederick N. Scatena, Sacramento, was reelected secretary-treasurer. Dr. Dan Sooy, formerly of San Francisco and now of Laguna Beach, was appointed to the Board by Governor Warren.

* * *

Announcing its annual cash award contest for 1949, the National Gastroenterological Association says that $100 and a certificate of merit will be given for the best unpublished contribution on gastroenterology or allied subjects. Certificates will also be awarded those physicians whose contributions are deemed worthy. Contestants residing in the United States must be members of the American Medical Association. Those residing in foreign countries must be members of a similar organization in their own country. The award for the winning manuscript is to be made at the annual convention banquet of the Association in October of 1949. The Association reserves the exclusive right of publishing the winning contribution, as well as those for which certificates of merit are given, in its official publication, *The Review Of Gastroenterology*. Entries should be limited to 5,000 words, be typewritten in English, prepared in manuscript form, submitted in five copies accompanied by an entry letter, and must be received not later than April 1, 1949. Entries should be addressed to the National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

* * *

Available free from local health officers throughout the state, a unique "Manual for the Control of Communicable Diseases in California" has just been issued by the State Department of Public Health. The booklet lists the communicable diseases in alphabetical order, and describes their significant aspects. Each section groups together the relevant California laws and regulations, information about laboratory diagnosis and the tests available from the State Division of Laboratories, recommended immunization procedures, the present status of specific therapy, and data on the role of the public health nurse. It is planned to revise the manual and correct any errors in approximately one year. To this end the State Health Department invites expressions of criticism and advice.

INFORMATION

Extra Pay, Choice in Assignment Offered by Army to Physicians Accepting Active Reserve Duty

Physicians who volunteer now for active duty in the Army Medical Corps Reserve will be given opportunity to select, within limitations, the place they wish to serve and the type of duty they desire, according to a spokesman for the Sixth Army Reserve.

These and other inducements are being offered to attract volunteers and thus avoid the need for the government to devise other means of procurement.

Increased pay to offset medical education expenses, initial appointment in advanced grades for those who qualify, a liberalized system of promotions, arrangements for internships and residencies, a minimum of administrative "paper" work, and retirement benefits for Reserve officers on active duty equal to those of regular career officers for the proportionate time served, plus some additional credits for time on inactive reserve status—these are among the new inducements offered (see chart, page 482).

Thirty physicians are needed between now and January 1, 1949, to fill Sixth Army requirements for California alone. An additional 60 must be recruited prior to June 1, 1949, and an undetermined number thereafter, according to need. Nationally, the Army's quota for 1949 is 4,000 physicians.

Volunteers may sign up for one, two or three year periods. During the first year of any volunteer service the physician will, where at all possible, be assigned to a post close to his home. The two and three year periods offer the opportunity to request foreign service in the theater of the physician's choice.

A communication from Sixth Army Headquarters in San Francisco details some of the problems:

"Enlargement of the Army due to the draft, and the completion of the tour of duty of the last of the Army School Training Program physicians and dentists, is causing a critical shortage of physicians and dentists for the armed forces.

"Since the Army is receiving the largest augmentation, its needs in this regard are more acute. To meet this situation at least until the government can find a satisfactory solution, we will need the active support of all members of civilian medicine and dentistry.

"We require, primarily, physicians and dentists for professional work in general hospitals, station hospitals, dispensaries and post dental clinics. It is highly desirable, from our standpoint, to secure these professional men on an officer status, and for a duty period of one year or more if possible.

"To solve this [problem of meeting the quotas] we must secure the active support of the whole broad base of medicine and dentistry in this country. . . . The opportunities for a professional man entering the regular service are better than at any previous time in the Medical Department's history. We have a professional training program second to none. Physicians and dentists on extended active duty, or in the Regular Army, receive $100 a month additional pay as compensation for previous professional training.

"We are utilizing these professional men entirely on professional work, and in the field of medicine or dentistry which they most desire, or, at least, have received training for, in civilian life. This is, of course, professionally desirable, administratively feasible, and also necessary to secure the greatest amount of professional service with the minimum of personnel. It also corrects one of the major criticisms of professional men who served during the war.

"For information on this subject, it is desired that you write the Surgeon, Headquarters, Sixth Army, Presidio of San Francisco, California, or contact the post surgeon at the nearest military installation."

The Relationship of the Practicing Physician to the School Health Program

DAVID VAN DER SLICE, M.D.*

Every practicing physician plays a part in the school health program whether or not he serves as a school physician. The medical services he gives to children in his private office are an integral and important aspect of the program. No program of health education in the schools can be wholly successful without the private physician's active participation and the approval and support of the local medical society.

The American Medical Association, recognizing the need for a closer relationship between the practicing physician and the schools, called a nationwide conference in October, 1947, on the Cooperation of the Physician in the School Health and Physical Education Program. Delegates from nearly every state medical association met with representatives from state departments of health and of education to explore ways in which the physician in private practice can best serve in the school health program. The conference unanimously recommended that "every local medical society set up a school health committee" to act in an advisory capacity to the schools with regard to the health program.† This was declared to be a necessary first

*School health consultant, State Department of Public Health.

†An alternate plan is for the public health committee of the Society to assume this function.

ESTIMATE OF EARNINGS—U. S. ARMY MEDICAL OFFICER WITH TWO DEPENDENTS

(Estimate of Earnings Based on Entrance Into Service at Lieutenant Grade)

Grade	Automatic Promotion Next Higher Grade (1)	Base Pay (2)	Medical Equalization Pay (3)	Allowance (4)	Retirement Benefits for Age (5)	Retirement Disability (6)	Death Gratuity (7)	Tax Differential (8)	Health Insurance (9)	Total Annual (10) (11)
LIEUTENANT	After four years of service	$2,400.00 No prior service	$1,200.00	$1,411.00	$1,050.00	$ 45.90	$13.40	$515.29	$102.00	**$ 6,737.59**
CAPTAIN	After eleven years' service	2,898.00 3 years' service	1,200.00	1,591.00	1,050.00	59.05	16.95	576.02	102.00	**7,493.04**
MAJOR	After eighteen years' service	3,960.00 12 years' service	1,200.00	2,026.50	1,050.00	100.24	27.58	748.07	102.00	**9,214.39**
LT. COLONEL	To Colonel by selection only	5,005.00 18 years' service	1,200.00	2,206.50	1,050.00	157.97	42.77	872.27	102.00	**10,636.51**
COLONEL	To General Officers by selection only	6,380.00 27 years' service	1,200.00	1,951.00	1,050.00	232.54	63.82	910.57	102.00	**11,889.93**

1. Unless he is promoted sooner which, under present conditions can be expected, an officer of the Medical Corps is automatically promoted to the next higher grade at the completion of years service in grade as shown.
2. Base pay is computed on average years service for pay purposes in each grade and is subject to a 5 per cent increase for each additional three years' service to a total of thirty years. Service, active or inactive, performed in any branch of the Armed Services at any time is credited for pay purposes.
3. Regular officers and reserve officers accepted for active duty for one year or more, on duty and appointed between 1 September 1947 and 31 August 1952. This payment limited to 30 years or total of $36,000.
4. Includes allowances for rent and subsistence.
5. Based on figures obtained from the Massachusetts Mutual and John Hancock life insurance companies. To purchase outright at age of sixty-four a life annuity comparable to Army retirement requires $60,000. Such an annuity purchased at age thirty requires $35,700 or thirty-four payments of $1,050. This is the figure shown in the table. The difference between $60,000 and $35,700 represents the amount of interest on the annual premiums and deductions made possible by the fact that a certain number of policy holders will die before the age of sixty-four. A policy taken out at an age earlier than thirty would of course have a lower annual premium. Reserve officers receive retirement pay at age sixty proportional to total active duty plus certain credit for inactive duty.
6. Cost of disability policy which pays benefit equal to Army disability retirement benefit. Based on figures from Acacia National Life Insurance Company.
7. Cost of insurance policy which pays at death, amount equal to Army six months, death gratuity. Based on figures from Acacia National Life Insurance Company.
8. Represents the income tax differential between an officer's salary and an equivalent civilian salary. Figures are based on deductions for subsistence, quarters, and the $1,500 special military exemption which is now effective and the continuation of which is expected in pending legislation.
9. The cost of a civilian health insurance policy providing benefits similar to those made available to an Army officer (Group Health Associations, Inc., figures as of 1 December 1946). There is no civilian policy which offers all the benefits available to an Army Medical Officer.
10. This table is not altogether complete because flight pay, parachutists pay, foreign service pay, commissary privileges, uniform and travel allowances, etc., are not included.
11. In addition to death gratuity pay the dependents of an officer who dies while on active duty from a service connected disease or injury is entitled to a pension, which in the case of a wife and two dependent children will be $720 or $1,380 annually, depending on whether death was due to conditions which developed during peace or war time service. A life annuity income paying such sums for a woman thirty years of age would cost $15,000 and $29,000 respectively.

step in achieving the practicing physician's cooperation and participation.

The schools need and welcome assistance from local practicing physicians in planning the school health program and in developing written policies and procedures patterned to fit local needs. The physician can make this contribution by serving on the advisory school health council.

The practicing physician renders one of his most important contributions to the school in his role of medical examiner, whether he sees the children in his private office or at the school. The medical examination gives the physician an opportunity to evaluate the pupil's health status in terms of physical and emotional growth and development, soundness of health practices and attitudes and general fitness to participate in the various school activities. Medical examinations of children performed at the school should demonstrate a high quality of medical service and be a satisfactory educational experience both to the child and his parent. An important objective is to develop an appreciation of and a desire for continued medical advice and guidance by the personal physician.

The chief purpose of medical examinations performed at the school is not to make a detailed diagnosis but rather to screen out any serious health problem which handicaps the child and, where indicated, impress upon the parent the importance of seeking further professional attention. The best place for the child to secure periodic medical examinations is in the office of his own physician who has previous knowledge of his health, has the facilities to make a thorough health appraisal and will give him continued health supervision. Experience has shown that when schools through an educational program and a definite administrative policy actively encourage pupils to obtain periodic medical examinations from their private physician, a majority of them do so.

The exchange of health information between the school and the physician has been demonstrated to be an important factor in safeguarding the health of the individual child. It is important that teachers know the physical limitations of their pupils; the physician, by sharing his knowledge about a pupil's health, can help the teachers to better understand their pupils and frequently enable them to assist in the solution of their health problems. It also permits an adaptation of the school program where this is necessary, for example, a restricted physical activity program for a child with rheumatic heart disease. The teachers must be made thoroughly aware of the necessity for safeguarding all matters of a confidential nature. A medical examination form, approved by the local medical society, would make possible the channeling of this useful information from the doctor's office to the school.

In recent years teachers have been trained to observe and record noticeable deviations from normal health and behavior in their pupils. Students suspected by the teacher—on the basis of her day by day observations—of having a health problem are referred through the medical department to their private physicians for medical examination. Certain of the information and impressions gained through the teacher's daily observations is very helpful to the physician responsible for medical supervision of the child. An exchange of information about pupils' health enables both physician and school to do a better job of health supervision.

Other ways in which the practicing physicians can contribute to the school health program include:

1. Giving medical guidance to the school's physical education program and to aid in developing uniform policies regarding excuses from physical education.

2. Assisting in a program of in-service education for teachers and school health service personnel.

3. Appraising the health content of the school curriculum in terms of factual accuracy and completeness of coverage.

Practicing physicians can make valuable contributions to the health of the community, as well as to the health of children under their private care, by taking an active part in the health program of the schools.

Diabetes Detection Drive

HOWARD F. ROOT, M.D., *Chairman,*
Committee on Diabetes Detection

The finding of the million unknown diabetics in this country poses a direct challenge to the American doctor. It is within his power to accomplish this feat. The existence of a million undiscovered diabetic patients in the United States has been demonstrated through a series of surveys, the most recent one conducted by the United States Public Health Service. The results of these studies now provide a springboard for organized medicine and a golden opportunity for physicians to seize the initiative *on their own* in this significant phase of public health.

The American Diabetes Association has planned a campaign to promote the early discovery and prompt treatment of the million undiscovered cases of diabetes. This campaign is unique in professional service, for according to plan the physician himself will be at the helm. Therefore, the plan cannot be prosecuted, or even started, without the endorsement and support of the entire medical profession through its governing bodies, national, state, county and local medical societies.

The plan proposed by the association is simple, direct, and sure. Through local diabetes associations, related to the American Diabetes Association and with cooperation of local, county and state medical societies over the United States and Canada, it is planned to carry out blood-sugar screening tests by a new five-minute micro-blood sugar method with simultaneous urinalysis for sugar with attention to the time in relation to the preceding meal. The procedure can be carried out apart from a formal labo-

ratory. The equipment is still in the manufacturers' hands but is to be available within two or three months. The only provision will be that the candidate must name a physician or clinic to which the results of the tests will be mailed for interpretation to the patient. *Under no condition* will a report be sent directly to the examinee. The effort is to bring the unknown diabetic patient under his own physician's care. There will be no statistics; no red tape.

Simultaneously, the American Diabetes Association will carry on an intensive educational campaign directed first toward doctors' post-graduate courses. It will be directed toward the layman by radio, newspapers and other publicity channels in addition to the *A.D.A. Forecast,* the Association's bi-monthly magazine which brings to the diabetic patient homespun articles on the disease by eminent authorities in the field. At the same time the association will place in the hands of physicians over the country an authentic "Handbook of Therapy." Containing the most up-to-date information available, the handbook will assist the physician in treating diabetic patients.

The week of December 6-12 was proclaimed as "Diabetes Week." This was the formal beginning, the kick-off, of the association's diabetes detection drive. From this start, the program will continue on a long-term basis.

The association is determined to do its part in finding these million individuals and guiding them to you, their physicians, for treatment. May we count on your support when the matter comes up before your county or local medical society? The success or failure of the diabetes detection drive depends upon you. *You* stand at the helm; this is *your* project.

BOOK REVIEWS

DIAGNOSIS IN GYNAECOLOGY—A Classification of Gynaecological Diseases Based on Aetiology and the Clinical Logic of Diagnosis. By James V. Ricci, A.B., M.D., Clinical Professor of Gynaecology and Obstetrics, New York Medical College. The Blakiston Company, Philadelphia & Toronto, 1948. 259 pp., no illustration.

This small volume resulted from efforts to teach gynecological history-taking and examination to undergraduate medical students at the New York Medical College. It may have some value in that connection, but its value to the practitioner seems doubtful. The author has taken information which is available in all of the standard gynecologic textbooks and rearranged it to suit his own devices. After brief descriptions of pelvic anatomy and embryology, as well as the female sex hormones, there follow many details about the performance of gynecological examinations. Under "special types of examination" there is no mention of the Papanicolaou smear technique. The rest of the volume concerns itself with classifying pelvic disorders on the basis of what the author insists upon spelling "aetiology." Throughout the book the diphthong is used also in the word "gynaecology." The author's concept of the meaning of the word etiology seems at variance with the generally accepted definition. One wonders what is gained, for example, by stating that "diseases of the uterus result from the following aetiologic factors" and then setting forth a list containing every conceivable uterine disorder, all the way from pyometra to bullet wound of the uterus. There is also some mention of pregnant uteri having been pierced by bulls' horns. Certainly this must occur infrequently in New York City. While the reviewer finds no serious errors of fact in this text, it seems fair to say that it contains very little information which will be of value outside the classroom from which it sprang.

* * *

PRACTICAL BACTERIOLOGY, HEMATOLOGY, AND PARASITOLOGY. By E. R. Stitt, M.D., Rear Admiral, Medical Corps, and Surgeon General, U. S. Navy, Retired; Paul W. Clough, M.D., Physician-in-Charge of the Diagnostic Clinic, Johns Hopkins Hospital; and Sara E. Branham, M.D., Senior Bacteriologist, National Institute of Health, and Contributors. Tenth Edition. The Blakiston Company, Philadelphia.

Republished for the first time since 1938, the tenth edition of this book, which was originally published by Rear Admiral E. R. Stitt in 1909 and since that time has been a very popular textbook covering principally the techniques of bacteriology, hematology, and parasitology, has been entirely revised by Stitt, Clough, and Branham and is contributed to by other authors.

Primarily a text on laboratory technique, it covers the various subjects in a complete and acceptable manner. It is particularly outstanding in the fields of bacteriology, serology, and parasitology. The section on diseases of the blood is excellent when viewed in the light of its obvious functions, but should not be confused with a reference text giving an exhaustive coverage of hematology.

Its outline and the manner in which much detail is presented continue to make it one of the most outstanding books in this field. The references to clinical applications, which form an integral part of each topic which is presented, increase its practicability. It must not be considered just a textbook for medical students and technicians. It is designed to fill a much greater function, and strengthened by the section covering the techniques of the examination of various body fluids and organs, it becomes a practical text, not only for those in the profession of medicine who routinely or occasionally perform laboratory procedures, but also for those research workers, clinicians, or teachers who are true medical scientists.

The material is well arranged in such manner that the text is readily usable for specific reference work. The bacteriology, immunology, hematology, and parasitology are very properly conveniently separated from each other with overlapping of material only for purposes of clarity and accuracy.

The book can heartily be recommended as a valuable text for students and as a useful guide and reference book for the practitioner of medicine.

* * *

MEDULLARY NAILING OF KUNTSCHER. By Lorenz Böhler, M.D., Director of the Hospital for Accidents in Vienna; Professor of Surgery at the University of Vienna. First English Edition revised by the author. Translated from the Eleventh German Edition by Hans Tretter, M.D., Surgeon in Charge of the New Jersey Manufacturers Hospital. The Williams & Wilkins Company, Baltimore. 1948. $7.00.

Like many other fracture surgeons Lorenz Böhler has always sought a simple method of internal fixation which could be applied *without opening the fracture site.* In 1940 Küntscher described such a method. This consists in the insertion of a long, hollow, strong steel (V_2A) rod through a small incision at one end of the bone down through the medullary canal across the fracture site deep into the distal fragment. When Böhler saw this procedure it appealed most strongly to him. Here at last was a simple method of securing internal fixation *without opening the fracture.* Thus the important fracture hematoma was preserved, risk of infection was practically nil, early muscle function and joint movement along with weight bearing was possible and finally *callus formation and fracture healing were accelerated.* It was fantastic. He quickly resolved to adopt the method. Anatomical studies were carried out to determine the exact width, length and direction of the medullary canals so that length, width and curve of nail could be accurately figured.

Two hundred sixty-eight cases have been operated upon in the Viennese Hospital for traumatic surgery. This series embraces not only fresh fractures of all the long bones, but includes many old ununited fractures, nonunions, malunions, pseudo-arthroses, bone shortening operations, spontaneous fractures, etc. In addition Böhler has had an opportunity to study the records, x-rays, patients, and end results of over 300 Küntscher nailing operations performed in other hospitals.

This extensive experience permits the author to describe in great detail the instruments and apparatus required, the exact technique for inserting the nail, the kind of case suitable for the method, the postoperative care, and the reasons for possible success or failure.

The method, which at first seemed so simple, has in fact turned out to be so complicated that it quite obviously can be used only by surgeons of great experience with much expensive and complicated apparatus available. For example, a fractured femur requires a specially designed traction frame, 36 special instruments or apparatus which includes two mobile fluoroscopic units, a fluoroscopist, x-ray technician and an anesthetist in addition to the surgeon, his assistants and the regular operating room nurses.

Careful study of over 600 cases has brought to light an "almost unbelievable number" of complications and end results. Death, comparatively frequent infection, faulty position of fragments, faulty position of nail, splitting bone with nail, rotation of fragments, migration of nail into joint, broken nail, and many others have been recorded.

Careful observation has proven that the massive spindle of callus seen in some of the earlier cases was in fact due either to the irritation resulting from corrosion of poor quality steel nails or to persistent slight movement at the fracture site (nail too short or too long). Such massive callus is of poor quality and in these cases actual fragment fusion is very slow. *Actually callus formation and fracture healing are somewhat impeded by the presence of the nail in the medullary canal.* This observation, verified by Maatz at the Kiel Clinic in 300 cases, "constitutes the greatest disappointment that I have experienced as a physician, because I had set the highest hopes upon the callus-stimulating effect of the medullary nail." Furthermore "it is evident that closed medullary nailing is suited chiefly for transverse fractures of the femur in the middle third." In addition, perhaps in the hands of certain expert bone surgeons, the nail can be used in selected cases of nonunion, where the fracture must be exposed to freshen the bone ends or insert grafts (open nailing), in bone shortening operations, and certain pathological fractures.

The book is highly recommended to all surgeons who treat fractures. It tells everything that is known about medullary nailing. The chapter on "callus" is a classic. Böhler's observations on the results of skeletal traction are sound and practical. These alone are worth the price of the book.

* * *

BRITISH SURGICAL PRACTICE VOL. I. Under the General Editorship of Sir Ernest Rock Carling, F.R.C.S., F.R.C.P., Consulting Surgeon, Westminster Hospital, and J. Paterson Ross, M.S., F.R.C.S., Surgeon and Director of Surgical Clinical Unit, St. Bartholomew's Hospital; Professor of Surgery, University of London. In Eight Volumes (With Index Volume). Butterworth & Co. (Publishers), Ltd., London, England. The C. V. Mosby Company, St. Louis, Mo., U.S.A., 1947. $15.00.

As one reviews this first volume of an eight-volume system of surgery, he is impressed by the very substantial, high quality paper upon which it is printed and by the consequent excellent appearance of its illustrations.

The subject matter is excellent, also, although one misses a brief historical resumé of the subject and, in certain disorders, a more detailed account of their pathologic physiology. Excellent suggestions as to treatment abound. What it lacks in a coherent, well-integrated account such as one expects from a textbook authored by a single person, it gains in the greater completeness and more authoritative treatment provided by numerous experts in their fields.

One is a little puzzled to find so many unrelated subjects covered in the same volume and to find "peripheral arterial diseases" included in the chapter devoted to the "autonomic nervous system" instead of under "arteries." When all eight volumes lie before one, however, reference to related conditions will undoubtedly be made easily and we trust without confusion, and without unnecessary repetitious accounts of the subject. One awaits the succeeding volumes with real anticipation that reading them will be amply rewarded.

* * *

THE NURSING OF TUBERCULOSIS. By O. V. Buxton, S.R.N., and P. M. Maculloch Mackay, S.R.M.N., with a Foreword by Richard R. Trail, M.C., M.D., Illustrated by Nora Lewis, S.R.N. John Wright & Sons, Ltd., Bristol, Simkin Marshall (1941), Ltd., London, 1947. $2.00.

In the preface of this brief volume the authors mention that it is "written expressly for the nurses and student nurses engaged in the nursing of tuberculous patients." The subject material is well covered. The illustrations are very helpful for the student.

As can be expected there is variation in terminology and spelling which may confuse student nurses. The indications listed for various procedures may also not agree with some of the teachings of American chest specialists. For this reason it may be advisable to recommend this book for graduate nurses interested in diseases of the chest rather than as a standard text for student nurses.

* * *

HANDBOOK OF OPHTHALMOLOGY. By Everett L. Goar, A.B., M.D., F.A.C.S., Professor of Ophthalmology, Baylor University College of Medicine, Houston, Texas. With 48 Text Illustrations and 7 Color Plates. St. Louis. The C. V. Mosby Company. 1948. $5.50.

This handbook of Ophthalmology is the result of the setting down of his lectures to medical students by the author. In so doing, he has given a brief description of the commoner means of examining the eye, and the commoner eye diseases. He has also very briefly mentioned methods of treating eye diseases without going into details. There are some excellent illustrations in the book which add to its value. It would make a good handbook for someone who wished a superficial knowledge of facts about ophthalmology without ever expecting to treat the eye.

* * *

PRACTICE OF ALLERGY. By Warren T. Vaughan, M.D., Richmond, Virginia. Revised by J. Harvey Black, M.D., Dallas, Texas. Second Edition. The C. V. Mosby Company, St. Louis. 1948. $15.00.

The publication of a Second Edition of Vaughan's Practice of Allergy with revisions by Dr. J. Harvey Black is of importance to the field of Allergy. The first edition of the Practice of Allergy appeared in 1939. Since then many books in this rapidly developing field have appeared but none possess the quality, flavor and distinction which its erudite author gave it. Warren Vaughan's book still remains a historical bridge between our old concepts of the underlying causes of allergic manifestations and our newer interpretations.

In common with all publications in so broad a field by a single author, it has the usual weakness, that no one author can write authoritatively on all phases of the subject. This has been partly overcome by the addition of a chapter on Pollen Surveys in the United States and Adjacent Areas and Field Surveys and Aerobiology by Oren C. Durham, an expert in the field. Dr. J. B. Howell has rewritten the chapter on Fungus Infection with Associated Allergy, a phase of allergy which needs much clarification. The chapter on Vital Capacity by Dr. James Holman is a brief but important addition to our understanding of the pathologic physiology of the respiratory mechanism in bronchial asthma.

Finally it should be stressed that there are few books on Allergic Diseases which present so clearly the original concepts of the late Dr. Vaughan on the Balanced Allergic State or Allergic Equilibrium and Food Groups. The revisionist is to be commended for retaining these in the vivid wording of the First Edition.

Since its first appearance in 1939, the reviewer has found Vaughan's Practice of Allergy an excellent reference book and he feels assured that it will be helpful as a guide, not only to the general practitioner but also to the specialist in Allergic Diseases.

* * *

SURGICAL DISORDERS OF THE CHEST. By J. K. Donaldson, B.S., M.D., Associate Professor of Surgery and in charge of Thoracic Surgery, University of Arkansas School of Medicine, Little Rock, Akansas. Second Edition, pp. 485, Lea and Febiger, Philadelphia, 1947. Price, $8.50.

The main additions to the first edition (1944), are concerned with a more detailed consideration of the advances in traumatic thoracic surgery made in World War II, the treatment of pleurisy, surgical diseases of the esophagus, and operations to correct congenital cardiovascular anomalies.

In his preface, the author states that the volume is primarily designed as a reference book for physicians, surgeons and medical students. He indicates that sufficient technical detail is included to permit the competent general surgeon to treat certain surgical disorders of the chest.

As the most recently published attempt to correlate what is new in surgery of the chest, the book is certainly worthy of serious consideration and careful study. Many medical students and physicians, not specialists, will find it a useful reference text. The inclusion of a chapter on resuscitation and inhalation therapy is a welcome addition to a surgical volume.

On the critical side several features of the book must be discussed. The over-all impression is that the text was written hurriedly. There are far too many references to other sections in the book, particularly following sections. This, combined with frequent parenthesized directions, makes for poor continuity both of text and of thought. Due either to carelessness in writing the original text or too hurried proofreading there are at least 40 examples of misspelled words, unwieldy English and misquoted statistics.

Frontal roentgenograms are not reproduced uniformly in position. Frequently they are inadequate, particularly the bronchograms. This may be due in part, however, to a poorer grade of paper in the second edition.

A few of the more obvious deficiencies in text should be listed. The important role of endoscopic procedures in diagnosis and treatment is nowhere emphasized sufficiently. The inference is made throughout that the thoracic surgeon usually does not perform his own endoscopies, an entirely unwarranted impression.

In general, the illustrations are adequate and many are excellent. Figure 107, page 324, is, however, extremely small and is confusing even to a surgeon with considerable knowledge of hilar anatomy. Unfortunately the colored plates on decortication lack third dimensional detail.

The following lesions should be discussed more completely: carcinoma of the upper esophagus; intrapulmonary cysts and emphysematous blebs; primary carcinoma of the lung and its differentiation from bronchial adenoma; traumatic diaphragmatic hernia.

The surgical therapy of pulmonary tuberculosis is covered rather sketchily. The reviewer disagrees with the expressed opinion that the objective of pneumothorax therapy is complete collapse of the lung (p. 376). The discussion of lobectomy and pneumonectomy in tuberculosis should certainly be enlarged.

Finally, a discussion and description of methods which are now obsolete add nothing to the practicability of a book designed primarily as a working manual for others than thoracic specialists. There are confusing allusions to tourniquet ligation in lobectomy and pneumonectomy. The inference that tourniquet ligation is *ever* indicated in pneumonectomy for carcinoma is challenged.

In conclusion, the rapid improvement of thoracic surgical techniques and the widened indications for operative interference in many thoracic diseases make it advisable that this material be assembled in available form. The author obviously has expended much effort in the preparation of the first and second editions. It is to be hoped that if a third edition is contemplated, more care will be exercised in obtaining smoothness and clarity; that pertinent additions and deletions will result in a more useful compendium.

ARTERIAL HYPERTENSION. By David Ayman, M.D., Instructor in Medicine, Tufts College Medical School. Edited by Henry A. Christian, A.M., M.D., Hersey Professor of the Theory and Practice of Physics, Emeritus, Harvard University. (Reprinted from Oxford Loose-Leaf Medicine with the same page numbers as in that work.) Oxford University Press, New York. $2.50.

David Ayman's publications over the past 20 years have made it clear that he is one of the foremost students of arterial hypertension as observed in patients; his earlier papers on the critical evaluation of therapeutic results in this disease are classics. In this short monograph he concisely gives his views as to etiology, pathological physiology and evolution of the disorder. Symptoms, physical and laboratory findings are well discussed, and above all there is a sound discussion of treatment (of psychoneurotic, vaso-spastic and organic symptoms, and of the elevated blood pressure itself). The author gives reasons for his belief in the value of thiocyanates and sympathectomy in lowering pressure levels.

A few minor criticisms may be ventured. The reviewer happens to disagree with Ayman's concept of the relation of hypertrophied myocardial fibers to heart failure, and with his use of the word "hypertrophy" in much of the discussion on x-ray of the heart. Adrenal medullary tumor is not acknowledged to be a cause of hypertension other than of the paroxysmal type.

These rather academic points should not obscure the fact that here is an outstanding work by an eminent authority, a work which every medical student, teacher and physician should read carefully and preferably own.

* * *

PROGRESS IN NEUROLOGY AND PSYCHIATRY—An Annual Review Vol. III. Edited by E. A. Spiegel, M.D., Professor and Head of the Department of Experimental Neurology, Temple University School of Medicine, Philadelphia, Pa. Grune & Stratton, New York, 1948. $10.00.

This review, the third in the annual series, maintains the high standard of quality shown by its predecessors. The fields of neurology and psychiatry are covered thoroughly in the 661 pages of the volume, of which 420 are devoted to neurology. As is natural in such a compendium, the quality of the individual reviews varies widely, from a scholarly critical account of recent work and thought on a subject, as exemplified by Schwab's article on Electroencephalography, to a rather prosaic cataloguing of relatively unrelated papers. In all, however, the work is readable and informative and, after its original perusal, constitutes a handy reference book to the recent literature. It can be recommended to the physician who wishes to keep abreast of current thought in this field.

* * *

PEDIATRICS FOR NURSES. By Arthur G. Watkins, M.D., F.R.C.P., Physician in Children's Diseases, Cardiff Royal Infirmary. Illustrated. The Williams and Wilkins Co., 1948. $3.50.

This book is an excellent reference book for nurses in the United States. It is written by a physician apparently without active collaboration of a nurse, which is contrary to the usual practice in our country. The book also particularly presents problems from the point of view of another country, which is always stimulating and refreshing. There is considerable variation in the types of diseases seen in different countries as well as in the approach to therapy. The book might be read with profit by medical students and resident physicians to acquaint themselves with procedures to be learned from the nursing profession.

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*R. H. Follis, D. Jackson, M. M. Eliot, and E. A. Park: Prevalence of rickets in children between two and fourteen years of age, Am. J. Dis. Child. 66:1-11, July 1943.

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